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Technology Review

Technology and Happiness

BY JAMES SUROWIECKI

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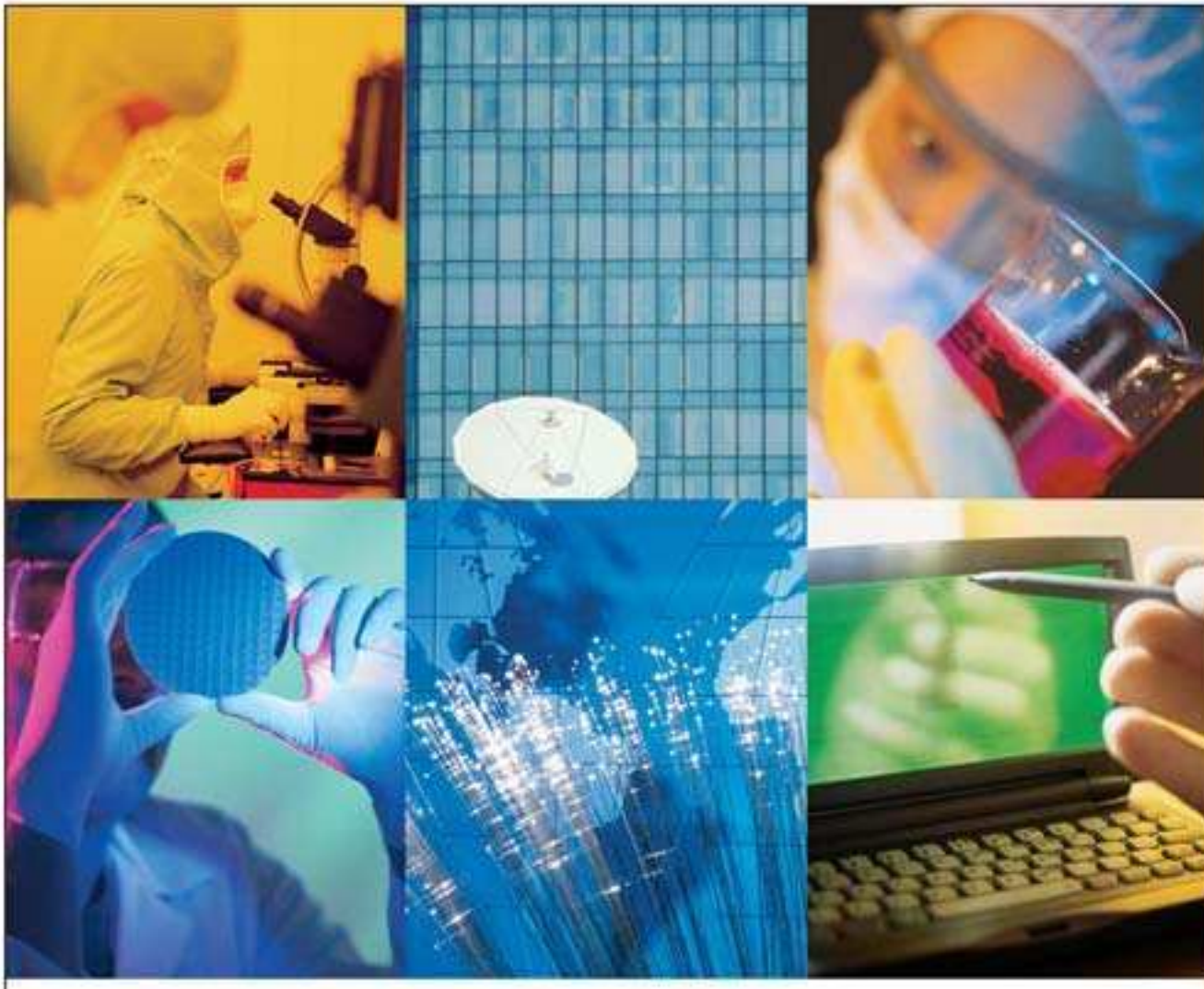

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Volume 108, Number 1

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COVER STORY

This could get ugly

Will Google 2004 be Netscape 1995 all over again? Everyone loves the search firm's technology. But there's reason to doubt that it's ready to compete with Microsoft. We asked Charles Ferguson, a legendary entrepreneur who, in 1995, sold Vermeer Technologies to Microsoft for $130 million, to explain the opportunity and danger that Google now faces.

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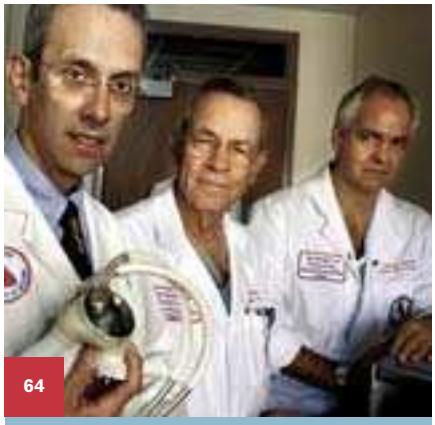

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This month on technologyreview.com

Our website—the daily destination for smart news about emerging technology—has a new look.

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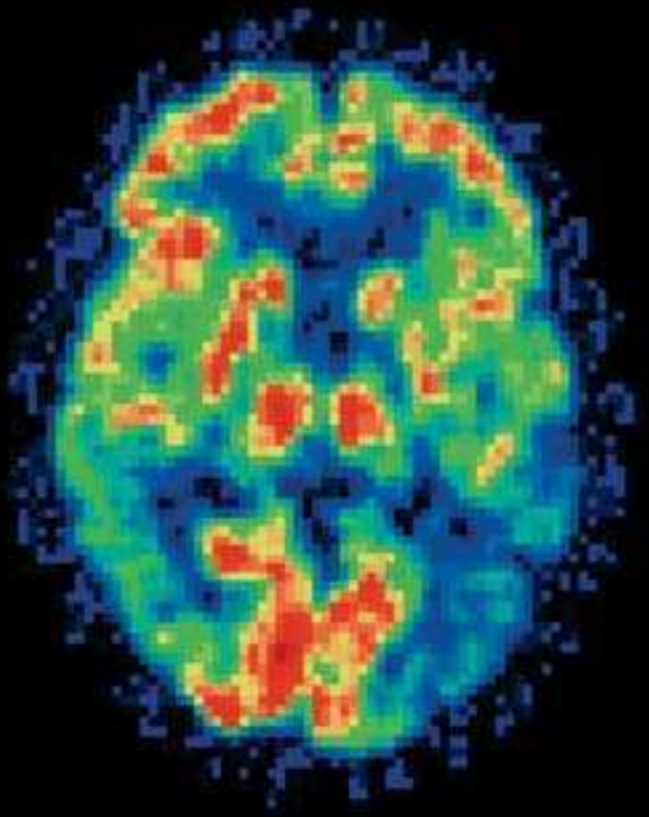

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What's Changed about *Technology Review?*

What have we done to your magazine?

This month, *Technology Review* introduces a new design, our first since 1998. Maybe no one besides editors and art directors is very interested in the details of magazine design: I will postpone a description of our new clothes until the end of this column. But a redesign is also an opportunity for the editors to reconsider the contents of their publication. *Technology Review* will be a different magazine—and our readers and advertisers may be interested in learning what we have changed and why we changed it.

Here's one thing that will not change: our subject matter. Since *Technology Review*'s founding in 1899, we have described emerging technologies and explained their impact. But with this redesign, we hope to do more.

WE WILL WRITE MORE. Our frequency, which has been 10 times a year, will increase to 12, and we will publish at least 20 more pages of journalism every issue.

OUR SCOPE WILL EXPAND. In other words, we will define technological "impact" more expansively. This month, you will see a few new sections. They include "Briefcase," case studies that examine how individual organizations succeed or fail in using new technologies; "Reviews," which seize upon a book, article, or report, the release of a product, or the occasion of an event to address some controversy; and "Synopses," which describe recent, important technological innovations or scientific articles and explain why they matter. Finally, at the very front of the magazine there is a kind of executive summary of our best articles called "readme." Each "readme" ends with a call to action: we tell you what you should do.

OUR ARTICLES, WHICH ARE GOOD NOW, WILL BE BETTER. We want our stories to be more thoughtful and analytical. We hope our style is clear, simple, and economical. We will avoid jargon and terms of trade. Among our biggest changes is *whom* we will publish. The journalists who write for us will be the very best: writers who are both experts in their fields and possessed of insight, observation, and wit. A good example is Sherwin Nuland, the author of next month's cover story, who has written a critical profile of Aubrey de Grey, a promoter of antiaging science at the University of Cambridge in England. Dr. Nuland is a professor of surgery at Yale, but he has also written for the *New Yorker* and won the 1994 National Book Award for *How We Die*. A word about our columnists: every month, we will invite a different technology celebrity to sound off in "Megaphone"; in "Megascope," Ed Tenner will write more soberly about the less obvious consequences of new technologies.

I hope that these remarks suggest our broader goal: we want *Technology Review* to be the best technology magazine in the world, and the one publication that everyone interested in technology must read.

And what of the design itself? We owe our new look to Roger Black and Jackie Goldberg of Danilo Black. Roger Black is perhaps the most famous living magazine designer, responsible for the designs of iconic publications as varied as *Rolling Stone*, *Esquire*, the *New York Times Magazine*, *Reader's Digest*, and *Foreign Affairs*, as well as the logos of *Time* and *Newsweek*. Very briefly, the design's main elements are:

A NEW TYPEFACE FOR OUR TEXT CALLED WALBAUM, a lesser-known Germanic cousin of the classic 18th-century fonts Bodoni and Didot; a new typeface of our own for headlines called Techbaum; and a new typeface for all navigational information called Akzidenz Grotesk.

SIMPLIFIED NAVIGATIONAL CUES THROUGHOUT THE MAGAZINE: whenever you open *Technology Review*, you should know where you are, what the section is for, and what any individual story is about.

A NEW EMPHASIS ON CHARTS AND INFORMATION GRAPHICS to represent econometric and scientific data. We know that you, our readers, were mostly trained as engineers, scientists, business managers, and financiers: you are accustomed to assimilating information as data, and you'd like to see the numbers upon which we base our analyses.

Bill Emmott, the editor of the *Economist*, in announcing his own magazine's redesign, once wrote, "Good design, like good writing, should blend into the background; it should be the servant of editors and readers alike, not their master." I could not say it better myself and will not try. Please write to me at jason.pontin@technologyreview.com, and tell me what you like or do not like about our design and new sections. ■

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Letters

TECHNOLOGY AND IRAQ

As a retired U.S. Navy officer and a communications subspecialist, I have an issue with the title of your article about the U.S. military's use of high-tech communications systems in Iraq ("How Tech Failed in Iraq," *TR* November 2004). Technology did not fail; some systems and equipment failed. There were inadequate channels, or the equipment was misdeployed. That doesn't mean the technology failed—only that different equipment should have been used. The article indicated that at the battle of Objective Peach, "old-fashioned training, better firepower, superior equipment, air support, and enemy incompetence" were the factors involved in the decimation of the Iraqi forces. However, it should be kept in mind that current "old-fashioned" training is the result of technological advances: better firepower, superior equipment, and air support capabilities. These factors improved and enhanced results, which made the enemy appear incompetent, as they were not at the same technological level. To imply that the technology failed is misleading.

Lt. Comdr. Howard B. Mirkin
U.S. Navy (Ret.)
Bangkok, Thailand

Thank you for closing the article as you did—with the reminder that ultimately, it is physical armor, not information, that is needed to protect troops in the field. I served in the active component as an armor officer and am now a reserve-component officer (quartermaster) running an IT consulting business. I was taught that nothing will ever replace boots on the ground. The intellectual debates between advances in technology and the need for ground troops who close with the enemy—a phrase common to all combat-arms missions—have gone on since the beginning of warfare. The comment about the alpha geeks and breakdown in command and control during the Iraq War led me to believe that a change in the organizational structure of military command might be favored.

Capt. Paul E. Lima
U.S. Army Reserve
Collegeville, PA

How is the incident described in this article conclusively a technology failure? It sounds more like a human failure than a technological one. How did spotting and reporting three whole brigades require anything more advanced than, say, WWII-era technology? It seems reasonable to assume that a maneuver element "at the very tip of the U.S. Army's final lunge north toward Baghdad," approaching a key strongpoint like that bridge, would've had some sort of reconnaissance available to it. If any air assets were available before 0300, they could've wrapped a note saying "Enemy in strength approaching objective" around a rock and dropped it on the battalion's position, dropped flares, sent a courier—something. I won't say there aren't problems with the technology, but from this article, I can't tell whether this is a reconnaissance failure, a communications problem, or command and control breakdown.

Bill McClain

TECHNOLOGY AND DEMOCRACY

I live in Texas and have presided over an election using Texas's version of an electronic voting machine. It worked well—much preferable to previous methods of voting. While it is true that other states have had problems with such machines, the answer is not to have the government own, maintain, and control them ("Technology and Democracy," *TR* November 2004). The recent Chavez election in Venezuela demonstrates the problems with a state-controlled system. Suitable standards should be established utilizing the best technology presently available. While it's essential to count the votes correctly, a more serious problem is ensuring that only U.S. citizens, having the proper documentation, be allowed to vote once, and only once, in each election. The proper use of technology can help us toward both goals.

John McCulloch
Austin, TX

I disagree completely with the contentions in Jason Pontin's editorial. Neither technology nor free-market economics is to blame for the expected chaos in voting; the system itself stinks. Dead people casting votes, illegal aliens doing balloting, and even multiple voting, regardless of electronic balloting—these are the documented facts of an increasingly corrupt system. However, the U.S. is still better than most other countries. Printing receipts of individual ballots for a paper trail is completely regressive; if a more logical and pertinent paper trail is wanted, keep paper ballots instead. Electronic voting is supposed to eliminate paper, not increase it! The solution: better election process procedures to deal with the cause of the system's massive corruption. Dealing with the mere mechanisms involved (balloting by any means) is useless and treats the effects, not the (true) cause of the problem. If any ballot were to be automatically connected to a valid and registered Social Security number that was electronically verified as accurate (to secure just one vote cast per authorized voter, per election), then that would be one method to secure proper balloting. Turning "electronic voting" into "a public utility, where the machines are owned and maintained by the state" will simply codify, rationalize, bureaucratize, and institutionalize the corruption within a corrupt system.

Joe Settanni
Windsor, CO

UNNECESSARY EXPONENTIALS

While I have no doubt that we will have the storage capability that Rodney Brooks cites in his column ("The Other Exponentials," *TR* November 2004), I question the need for such capacity given another premise in the column, namely that we will "live always connected broadband lives." Given the ability to stream content through the Internet to smaller, lighter devices, is there really the need to keep the content locally? I would be just as happy if the playlist on my iPod made a connection to iTunes and streamed the songs to the player on demand. I have already made such a transition: I am using several hundred gigabytes of storage attached to a wireless router to serve all the computers in my home. The individual computers no longer need to have huge amounts of storage.

Donald Hawk
King of Prussia, PA

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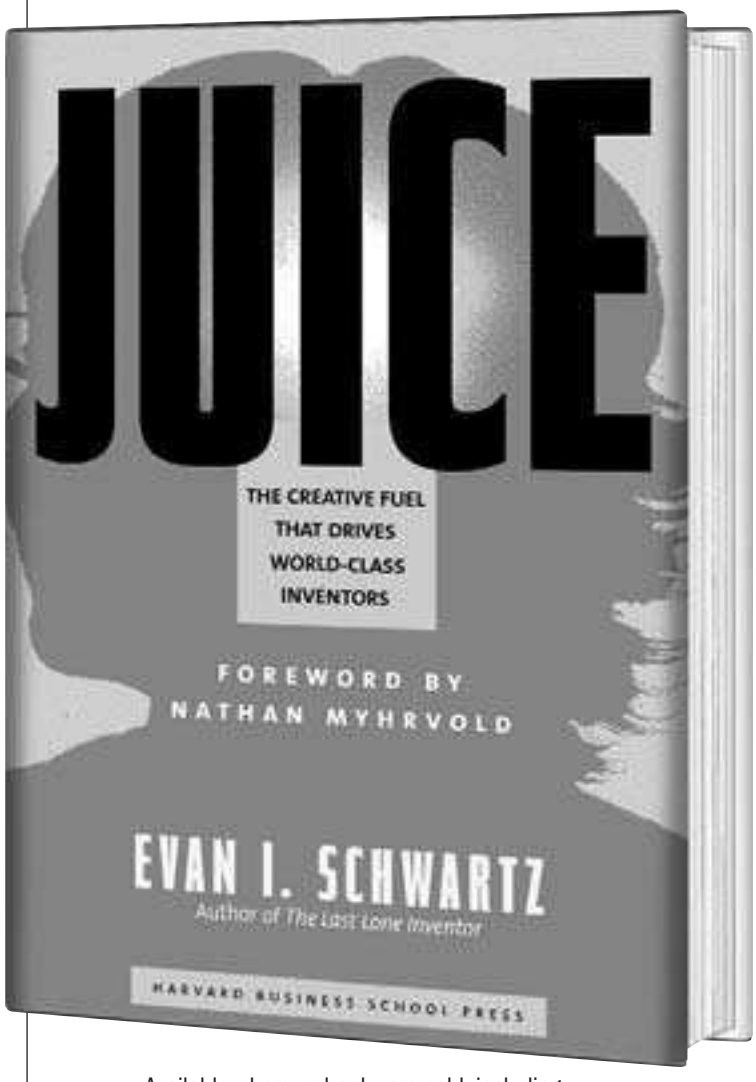

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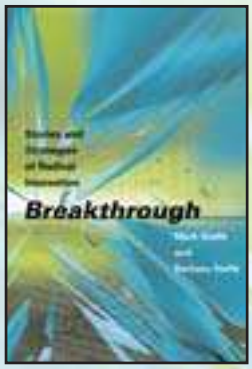

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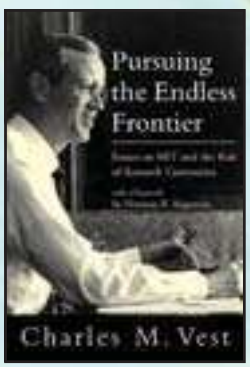

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foreword by Norman B. Augustine

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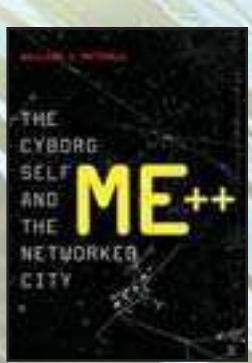

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Google: Be a Little Evil

Google is now such a boon to Web users that it's tempting to daydream about a real-world version of a perfect, all-knowing search engine. Why can't we Google our drawers for the counterparts to those mateless socks, Google the parking lot to remember where we left the Volkswagen beater—or Google the neighborhood to see who's looking for a used car?

As it turns out, Google's aspirations run in that direction: the company says its mission is to "organize the world's information." Already, it has branched out beyond Web searching to help users find information in product databases, e-mail archives, and their own hard drives. And having gathered $1.67 billion from happy investors on the first day of its public offering last August, Google can afford to take its innovative search technology a long way further.

But will it get the opportunity? As writer and entrepreneur Charles Ferguson spells out in the pages ahead, Google's ambitions put it on an irreversible collision course with Microsoft *(see "What's Next for Google?" p. 38)*. Though the software colossus is only beginning to mobilize on the search front, it is sure to come up with technologies that exploit its market-dominating operating system, desktop productivity software, and Web browser, so that search becomes a one-stop shopping experience for owners of Windows PCs.

If need be, Microsoft can outspend Google 30 times over on search-technology R&D. And that puts Google, despite its surging revenues and leading share of the search market, in a position disturbingly similar to that of Netscape in 1995. If it is to flourish—no, survive—Google must avoid the mistakes made by Microsoft's previous victims and mount a campaign to make its search technology into a global standard.

It has already started, by giving outside programmers basic tools for interfacing with its search database and, most recently, for adding features to its highly useful Google Deskbar. It can do more. To turn Google into a true platform for a whole universe of search services—in the same way that Windows is a platform for thousands of third-party PC applications—the company must create much more sophisticated tools for accessing its global network of servers, as Amazon is busily doing *(see "Amazon: Giving Away the Store," p. 28)*.

Google's corporate motto is "Don't be evil." Employees of Google apparently take this to mean "Don't be like Microsoft." Thanks to its dominance in desktop operating systems, Web browsers, and office software, Microsoft is able to impose proprietary standards to which all other developers of Windows software must conform, and this has earned the company a great deal of resentment from both software users and software developers. Developers would prefer to create better software than the Windows franchise allows. Users would like to buy better products. If it promoted its own proprietary-but-open standards for search-related functions, Google might suffer some minor damage to its image of innocence—but it would also secure its place at the center of the search business and provide an entirely new sphere for software innovation.

So if Google is serious about being the world's information gateway, it needs to start thinking a bit more like Microsoft. Ev-

eryone who uses the Internet should hope that happens—if only because software is better in markets where Microsoft has serious competition. Google must learn to be a little evil. ■

HAPPINESS

Don't Buy That New Gadget

72

Money can't buy happiness. Technology won't help either.

Does technology make us happy? Technologists, businesspeople, and most politicians assume so, celebrating its ability to improve our persons, experiences, and material circumstances. And ordinary human behavior seems to answer the question: if technology doesn't make us happy, why do we spend so much time, effort and money developing and buying all the stuff?

But the answer is not so simple, as James Surowiecki explains in "Technology and Happiness," on page 72. People are irrational about what will promote their well-being, and they aren't very good at anticipating their future preferences. Considering how many decisions about choosing new technologies are based on little (or even erroneous) information, perhaps we sometimes get stuck with technologies that don't make us happy.

The social sciences have been nearly silent on the subject. Since 1974, however, when Richard Easterlin published an article titled "Does Economic Growth Improve the Human Lot?", and more frequently in the last decade, economists *have* turned their attention to the vexing question of the complex relationship between wealth and happiness. Some of their insights can also be usefully applied to technology.

> When international phone calls, jet travel, or broadband access first appeared, they were wonderful things.

Easterlin and his disciples have demonstrated that while there is a strong correlation between poverty and misery, you can't buy happiness. Despite the fantastic increase in the prosperity of the United States since World War II, most Americans are no happier today than they were in 1947 (when happiness surveys began). Indeed, according to social scientists, the numbers of Americans who say they are "very happy" has actually fallen since the 1970s, even while the average income of someone born in 1940 has increased 116 percent. It turns out that when everyone's income swells, people's subjective sense of what they minimally require to be happy inflates, too.

Psychologists call this "hedonic adaptation"—and it works for technology as well. We become desensitized to our good fortune. When international telephone calls, jet travel, or broadband Internet access first appeared, they were wonderful things that seem to clearly make our lives better, but as their price fell and they became commonly available, they quickly seemed quotidian. In no time at all, we were irritated when they did not work perfectly.

So are we happier for new technologies? In one sense, Sure (imagine yourself, hedonically adapted to this world, stripped of all your stuff). In another sense, No. Happiness economists have shown that there is a kind of decreasing return to increasing income. Except for the very wealthy (the *Forbes* 400 consistently report that they are very cheerful indeed), people who strive ardently to become richer don't report any significant increase in well-being. Some happiness economists suggest that "inconspicuous consumption"—that is, investment in health, family, or community—tends to have a better return in happiness than buying bigger cars or houses.

It is the same with new technologies. Purchasing lots of the latest gadgets is unsatisfying: you know that in a few months there will be new, improved versions of the things. But some technology consumption is less conspicuous. Internet technologies like search or social networking are informational and affective networks that expand our knowledge and relationships. Biotechnology and health care offer a better and longer life. They're the better buy. ■

NASA

To Mars, by Tortoise

78

The US finally has a real plan for space exploration: go slow.

In November, engineers at NASA's Dryden Flight Research Center in Edwards, CA, conducted their third and final test of the X-43A scramjet—an unpiloted "supersonic combustion ramjet" that reached speeds of nearly Mach 10. The beauty of a scramjet is that it has none of the moving parts that compress air for combustion in a conventional jet; instead, the air is compressed by the vehicle's own forward motion. This also gives scramjets a big advantage over rockets, which must carry their own oxygen aloft in heavy tanks.

The X-43A's purpose was merely to prove the concept of hypersonic flight. But NASA believes future scramjets could be part of a next-generation system for launching piloted vehicles into space—and that makes the Dryden tests one hopeful sign that NASA's program of human space exploration is rousing itself from its 30-year slumber. Not since February 8, 1974, when Skylab was abandoned by its third crew, has the United States had a continuous, purposeful human presence in space. The Interna-

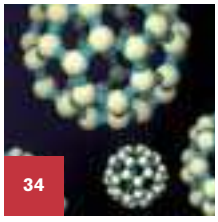
tional Space Station hardly counts: thanks to the grounding of the remaining space shuttles, it's halted in mid-construction and has a crew of two whose main job is to keep it from falling apart. Crew members come and go in Soviet-era Soyuz capsules. The shuttles themselves are a post-Apollo joke—$2 billion behemoths that, until the space station, had nowhere to go and nothing much to carry. They have also proved unacceptably dangerous, killing 14 astronauts since their initial flight in 1981.

It is time for a fresh start. If there is a post–Cold War rationale for sending humans into space—and Mark Williams argues in our new "Reviews" section that there is (see p. 78)—then Apollo-style crash projects and bloated, bureaucratized, cart-before-the-horse boondoggles like the shuttle program are not the way to put them there. Creating a permanent foundation for human exploration of the solar system will require a patient, incremental effort with tangible, science-driven goals—say, returning to the moon by 2020 and sending humans to Mars by 2050. In fact, this is the plan proposed by NASA and endorsed by President Bush last year. The first step will be the construction of a safer, simpler, Crew Exploration Vehicle (CEV) that can ascend to the space station, finally allowing NASA to send *Discovery*, *Atlantis*, and *Endeavour* off to the Smithsonian, where they belong. A second-generation lunar CEV would be built in orbit, whence rocketing on to the moon requires much less energy. The moon would then be the staging area for a third-generation CEV designed for the much longer trip to Mars.

There are, of course, enormous problems to be solved before this plan can proceed, such as how to shield interplanetary explorers from deadly solar and cosmic radiation and how to counter the debilitating effects of long-term weightlessness. But if NASA and international partners were to undertake a measured effort, with realistic milestones that spread the costs over a period of decades, then people under 40—few of whom have any memory of Apollo—may yet live to see a Mars landing. ■

NANOTECH

Real Benefits, Real Risks



The toxicity of nanoparticles needs further study

Fullerenes, better known as buckyballs, have been the darlings of chemists ever since they were discovered two decades ago. These novel molecules are, after all, a third major form of carbon, in addition to diamonds and graphite. Shaped like tiny geodesic domes, they also have an undeniable elegance. In recent years, they have emerged as one of the most valuable materials in the rapidly developing field of nanotechnology. But during the last year, preliminary toxicity studies on buckyballs have set off warnings about their potential health hazards.

Concern about buckyballs is part of a more general uncertainty about the safety of nanomaterials. The worry is that nanoparticles can, among other things, easily penetrate cells, producing unknown effects. Indeed, a few enlightened nanotechnologists, notably those at Rice University's Center for Biological and Environmental Nanotechnology (CBEN), have for several years been calling for further research on the biological effects of nanomaterials. Given the potential dangers, it makes good business sense that Mitsubishi, which is investing heavily in the manufacturing of fullerenes, has been actively dealing with the issue, working closely with Japanese authorities *(see "Mitsubishi: Out Front in Nanotech," p. 34)*.

> Worries over nanorobots are ridiculous; fears about the health risks of buckyballs are not.

The problem is that Mitsubishi and Rice's CBEN are the exceptions. The rest of the nanotech research community needs to recognize that toxicity questions are serious and cannot be ignored. No one knows what dangers may or may not exist. Expensive and time-consuming toxicity studies need to be done. Nanotechnology holds great promise: buckyballs are beginning to find uses in cancer drugs and solar cells, while other nanomaterials, such as carbon nanotubes, are likely to be even more useful. But for nanotech to go ahead, the public must be confident about the safety of these materials.

Much depends on the public's understanding the real dangers. Worries over swarming non-existent nanorobots are ridiculous; fears about the health risks of buckyballs are not necessarily misplaced. (Last spring, a study showed buckyballs can cause brain damage in fish.) Those outside the nanotech community also need a better sense of the potential value of the technology. Public opposition to genetically modified organisms took root largely because few could see any compelling advantage to biotech crops such as herbicide-resistant soybeans. The lesson is simple: if industry wants consumers to accept risks, however small, it must show the public some tangible, substantial benefits. The nanotech industry would be well advised to keep focused on applications, such as cancer drugs and solar power, whose eventual payoffs are obvious.

The U.S. government has begun to invest money in understanding the risks of nanomaterials. The 2004 budgets of federal agencies participating in the U.S. National Nanotechnology Initiative included $106 million for research on the health and environmental issues related to nanomaterials. That's a good first step. But definitive answers about the toxicity of various nanomaterials could take years. The government must not wait; it must begin now to formulate appropriate regulations to ensure the safe handling and use of nanomaterials. The two industries in which fullerenes are likely to have the most significant impact, pharmaceuticals and chemicals, are among the nation's most highly regulated sectors. And rightly so: the public wants safe drugs and protection from hazardous chemicals. Nanomaterials should be included in this regulatory framework. ■

The U.K. Banks on Stem Cells

Will the U.S. be forced to cash out?

IN January 2001, the British Parliament passed a bill that authorized government funding for human embryonic stem cell research. Seven months later, in his first televised address to the nation, President George W. Bush pledged to do the opposite. By executive order, he denied federal funding for all research involving the creation of new human embryonic stem cell lines. Stem cell researchers who accepted federal dollars would be limited to working with a small number of officially recognized preexisting lines.

Bush made his decision for moral reasons: he wanted to discourage "further destruction of human embryos that have at least the potential for life." Regardless of whether the funding ban has accomplished that aim—and critics believe it has had the opposite effect—it has had a profound impact on a field that proponents believe holds the possibility of cures for Parkinson's disease, paralysis, diabetes, and a host of other ailments.

Underlying Bush's policy was the assumption that by knotting the purse strings of the National Institutes of Health (NIH), he could block a controversial avenue of research. To some extent, he was right. Although private industry stepped in to fill the vacuum left by the retracted federal funds, embryonic stem cell research in the United States has become fragmented. In the last four years, researchers have published few papers, prominent scientists have fled overseas, and, veteran researchers say, young scientists have become increasingly reluctant to enter the field. In the same span of time, Prime Minister Tony Blair has created an entirely different environment for stem cells in his country,

PETER STEMMLER

establishing regulatory and financial control over all research relating to the technology. Blair's stated intention is to not only help Britain's fledgling biotech industry but also ensure that British stem cell research is subject to ethical oversight.

The centerpiece of the British plan is a national stem cell bank, launched in September 2002. Based in South Mimms, a suburb of London, the bank is designed to serve as a clearinghouse for all British stem cells, vouching for their genetic stability, cultivating large standardized stocks, and ensuring their ethical use. Before U.K. scientists may even attempt to derive human embryonic stem cell lines, they must secure a government license. Furthermore, the terms of governmental funding require that scientists deposit their cell lines in the bank, so other researchers can work with them as well. The bank distributes the cells free of charge under the strict supervision of a motley panel of scientists, civil servants, and ethicists.

> "If you let private money get involved you end up destroying a lot *more* embryos."

Heike Weber, program manager at the U.K. Medical Research Council, the bank's main funder, explains the philosophy behind the bank's processes: "Stem cells are a public resource. We need to make sure that this research is done in an ethical manner and that once the lines are created, they are made available to other researchers. If you let private money get involved, then pretty soon you're going to have companies that don't want to share their lines, and you end up destroying a lot *more* embryos."

That's exactly what many believe has happened in the United States under Bush's executive order, but as the president embarks on his second term this month, there is little chance that he will alter his policy. And in Bush's second term, U.S. stem cell researchers will likely fall further behind not only their British counterparts but also those in Japan and Israel—countries that, like the U.K., have invested wholeheartedly in stem cell technology.

Currently, the best hope for American stem cell scientists lies outside the dominion of the federal government. In November, Californian voters passed Proposition 71 by a margin of 59 percent to 41 percent. The ballot measure calls for the state to invest $3 billion in stem cell research over the course of the next decade. But the new California Institute for Regenerative Medicine, established by the measure, will remain a deeply imperfect solution. The 29-member board that is in charge of distributing the research grants will be subject to almost no governmental or ethical oversight. And California has no plans to establish a stem cell bank.

Elsewhere in the United States, many researchers fear that private money will no longer be able to shoulder the burden of stem cell research. According to Eve Herold of the Stem Cell Research Foundation, a nonprofit group in Clarksburg, MD, "A lot of biotech companies [doing stem cell research] are having trouble raising capital right now. Not only is the legislative situation uncertain, but most of the research we need is basic biomedical stuff. We're not at the stage yet where investors can expect to have a marketable medical advance. A pall has been cast over the whole field."

Doug Melton, codirector of the Harvard Stem Cell Institute, believes that it is time the U.S. government offers stem cell researchers a new compromise. Don't fund the derivation of new embryonic lines he says, but let scientists study stem cells "wherever they were derived, provided the cells were obtained in an ethically acceptable fashion."

Launching a national stem cell bank like Britain's would be one way to ensure that U.S. stem cell research proceeds in a way that is fair and ethical, and which maximizes the benefit to public health. "This is something I and others suggested at least three years ago and on numerous occasions," says Melton, whose group recently announced the creation of 17 new human embryonic-stem-cell lines, all made with independent funding. "The NIH and [secretary of health and human services] Tommy Thompson have never given a good reason for not doing this. Oddly, they pay millions, literally, to companies—some of which are not in the U.S.—to distribute the 'official lines.' Go figure." If a national bank were established, Melton says, he would happily donate his lab's cell lines. In the meantime, he's finalizing arrangements to ship them off to South Mimms. **JONAH LEHRER**

PROTOTYPE

Sensitive Dust

Checking the dust on a door sill is an age-old way to see how clean a house is. Now researchers from the University of California, San Diego, are using specially engineered "dust" to see how clean the environment is. Chemistry professor Michael Sailor and graduate student Jamie Link have engineered small, glittery grains of silicon, about 100 micrometers on a side, that change color when they come into contact with organic pollutants in the air or water. Each particle is riddled with tiny pores that are coated with compounds that attract pollutants. As pollutants are drawn into the pores, the reflective properties of the particle change, producing a color shift that can be detected with a handheld reader up to 30 meters away. The researchers, who've licensed the technology to an undisclosed company, are working on particles tuned to a host of specific pollutants, so a user could simply toss out a handful of the dust to see immediately what, if anything, had poisoned the air.

Silicon particles make a drop of an organic pollutant instantly visible.

JAMIE LINK/UC SAN DIEGO

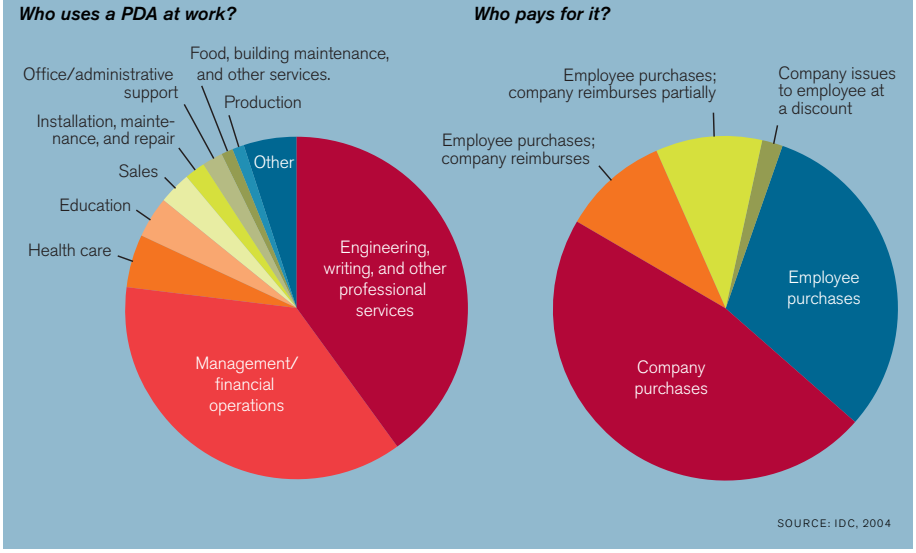
SOUNDBITE

"[Search] is something of a holy war for Microsoft—and one they can't bear to lose." *(see p. 38)*

MOBILE COMPUTING

In the Workplace, It's BYO PDA

Personal digital assistants increasingly constitute an ad hoc component of the workplace information infrastructure—and are often unsupported, unintegrated, and insecure. Eighty percent of nurses, for example, purchase their own PDAs to use on the job, according to a Spyglass Consulting Group survey. They're not alone: research by IDC shows that only about half of companies are footing the whole bill for workers who use handheld devices.



SOURCE: IDC, 2004

FACTS MACHINE

Air Cargo Insecurity

- **11.3 million metric tons** of cargo passed through U.S. airports in 2003.
- Less than **10 percent** of it was screened for explosives.
- **100 percent** of air passengers and their baggage are screened for explosives.
- Virtually all passenger flights carry air cargo.
- American Airlines spent **$70 million** to provide more legroom in coach class.
- Boeing spent **$1 billion** to launch a satellite-powered, high-speed in-flight Internet service.
- The U.S. Department of Homeland Security will spend **$4.8 billion** this year on passenger and baggage screening.
- It will spend **$115 million** on air cargo security.
- Last year, **two-thirds** of the U.S. Department of Homeland Security's transportation security R&D budget went to technology for countering attacks on commercial aircraft with shoulder-launched surface-to-air missiles.
- The United States has **6.3 million kilometers** of roads, more than **160,000 kilometers** of rail, nearly **600,000** bridges, more than **300** ports, and approximately **500** railroad stations.

SOURCES: U.S. TRANSPORTATION SECURITY ADMINISTRATION, ABI RESEARCH, BOEING COMMERCIAL AIRPLANES GROUP, GAO, U.S. DEPARTMENT OF HOMELAND SECURITY, AND AMERICAN AIRLINES

BIOTECH Q&A

Drug Development Is Virtually Dead

Genomics technology and science were supposed to unleash a cornucopia of powerful new drugs. Bill Haseltine—who stepped down in October as the chairman and CEO of Rockville, MD–based Human Genome Sciences—explains why that hasn't happened.

By all accounts, massive investments in genomics-based drug research haven't paid off. Why?
Productivity has actually declined at virtually every big pharmaceutical company. We've traded constraints on drug discovery for constraints on drug development.

Was the promise of genomics-based tools oversold?
It's not a science question. The current methods of drug development are still structured for another age.

You have a better idea?
Outsource the whole process to specialists—discovery, development, manufacturing, clinical trials. The skills that used to be housed in a few big pharmaceutical companies are now widely distributed around the globe. You manage it with contracts.

So do what a lot of the semiconductor industry has done—go virtual?
Drug targets are best developed based on scientific knowledge, which generally means an academic setting. A virtual or semivirtual company can take a group of those and coördinate the best providers at each stage, wherever they are. Most industries began seeing this long ago. That's where I want to put my energy now.

Would you go offshore?
They're doing great work now in China, India, and Eastern Europe. And in many disease categories, you don't want to do trials in the United States because there are simply not enough patients, and the FDA is—I don't think "obstructionist" is quite the right word, but in practice, that is the effect.

Alzheimer's research—you've been banging a drum for it. Anything to do with turning 60?
Alzheimer's is where AIDS was in 1985—the fundamental knowledge base is there. But whereas with AIDS there may be ten different therapeutic approaches, we have twice that number for Alzheimer's. It's a problem that's ready to be solved.

SPENCER REISS

PROFILE

Larry Sanger's Knowledge Free-for-All

Can one balance anarchy and accuracy?

WIKIPEDIA is the world's newest, largest, most varied, most participatory, and most controversial encyclopedia. It is composed and edited entirely by volunteer netizens; as of November 2004, there were some 29,000 "Wikipedians" writing for it in 109 different languages. The site's massive archive, including 380,000 articles in English alone, puts even Britannica to shame. If you don't see an article addressing your passion for miniature-teapot collecting, don't fret. Just write one.

Among Wikipedia's many unusual aspects is that its cocreator, Larry Sanger, is a professional epistemologist—a philosopher who explores the very nature and sources of knowledge and who, like many before him, once questioned the possibility of knowing anything with certainty. Sanger says that as a bookish teenager growing up in Anchorage, AK, he decided to model himself after Descartes and become a devout doubter, believing only the things that he could directly perceive or that could be logically derived from what he perceived. "These were the thoughts of a 17-year-old," smiles Sanger, who's now 36. But eventually, he says, he began to realize that some truths cannot be observed: "If the very project of seeking the truth required that I assumed something, then I would assume that."

This more pragmatic view sustained him through his college and graduate years as a philosophy student and even became the focus of his dissertation. But by that time, Sanger says, he was also becoming intrigued by the Internet and its possibilities as a publishing medium. And this convergence of interests helped him to realize that a newly invented type of website called a wiki—a forum that "allows a user to add content...but also allows that content to be edited by any other user," to quote the Wikipedia definition—could be used to assemble the contributions of thousands of amateurs into a reasonably truthful online encyclopedia.

How? "The subject of an encyclopedia is *received* knowledge," Sanger says, not absolute knowledge. The former, he says, consists of "the sort of claims one can make in the form 'It is generally known that....' It could be false, but it could still be 'generally known,' in the sense that people thought it was true." This idea underlay the nonbias policy that Sanger instituted for Nupedia, the expert-written online encyclopedia he was hired to edit in 2000. The policy says that contentious subjects should be described in a way that fairly represents every party's point of view. Wikipedia kept the policy when it spun off of Nupedia, and Sanger cites it as a main reason for the new site's success.

Nonbias is a difficult ideal to live up to. Indeed, the most common complaint against Wikipedia is that it is unreliable; since anyone can publish or edit any article instantly, there's nothing except the diligence of other contributors to keep favoritism, misinformation, vandalism, or sheer stupidity out of the encyclopedia's pages. But Wikipedia's "staff" of volunteers is "better than any full-time staff you could imagine, because there are so many people involved," Sanger says. Any malicious or mistaken entry "is going to be instantly noticed" and corrected.

But there's a second complaint against Wikipedia that bothers Sanger more deeply—the fractiousness among Wikipedians themselves. Sanger says participants often become embroiled in "revert wars" in which overprotective authors undo the changes others try to make to their articles. He says he's afraid that this kind of behavior drives away academics and other experts whose contributions would otherwise raise Wikipedia's quality.

Sanger may be speaking from the heart. He left Wikipedia in 2002 when funding for his position ran out and no longer contributes, in part because of the lingering sting of some particularly nasty revert wars. He now lives in a suburb of Columbus, and lectures in the philosophy department at Ohio State University, his alma mater. To build a public encyclopedia, you don't need faith in the possibility of knowledge, he says. "What you have to have faith in is human beings being able to work together." **WADE ROUSH**

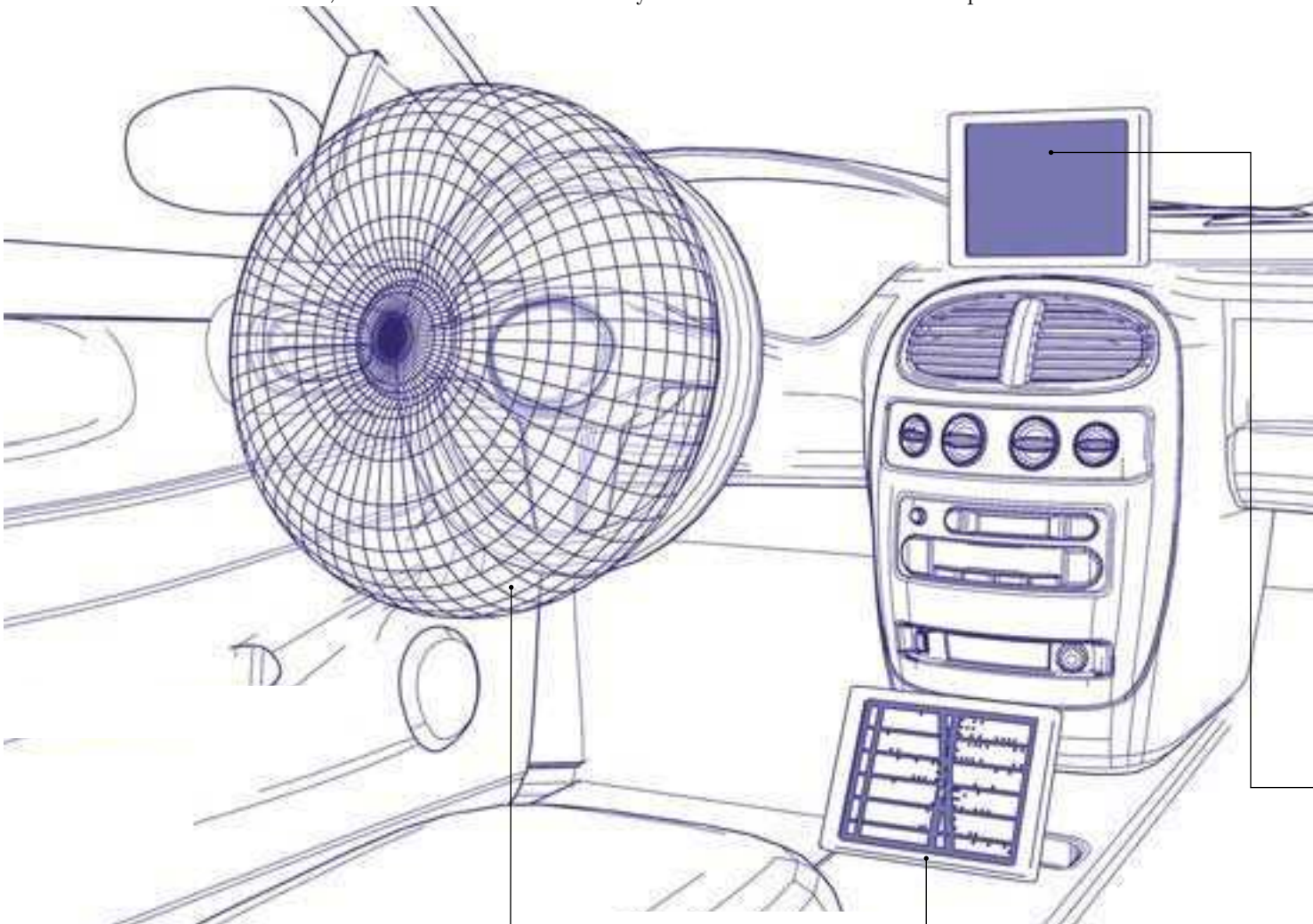
STEPHEN WEBSTER

CONSUMER TECHNOLOGY

Wireless on Wheels

Carmakers are taking telematics to the streets

AUTOMAKERS are loading new cars with an array of wireless communications and computing technologies, known collectively as telematics. But despite the unending variety of safety, convenience, and entertainment features telematics can enable, it has thus far held little appeal outside the United States; even in the United States, only 2.2 million of 17.7 million new automobiles were equipped with telematics in 2003. The number of North American subscribers to telematics services, however, is projected to increase by a factor of five over the next five years. No wonder General Motors is incorporating the technology into more than 50 of its models. And this year marks the debut on the U.S. market of cars from Japanese automakers equipped with telematics systems developed in house. Here are some of the latest telematics features from these and other car companies. **STACY LAWRENCE**



Emergency notification services

Telematics consumers are overwhelmingly drawn to services that will enhance their security and safety. Both OnStar and fellow telematics firm ATX Technologies offer such services: in the event that an air bag inflates, for instance, each system automatically alerts an operator who can call for an ambulance. The systems can also track stolen vehicles and unlock doors remotely.

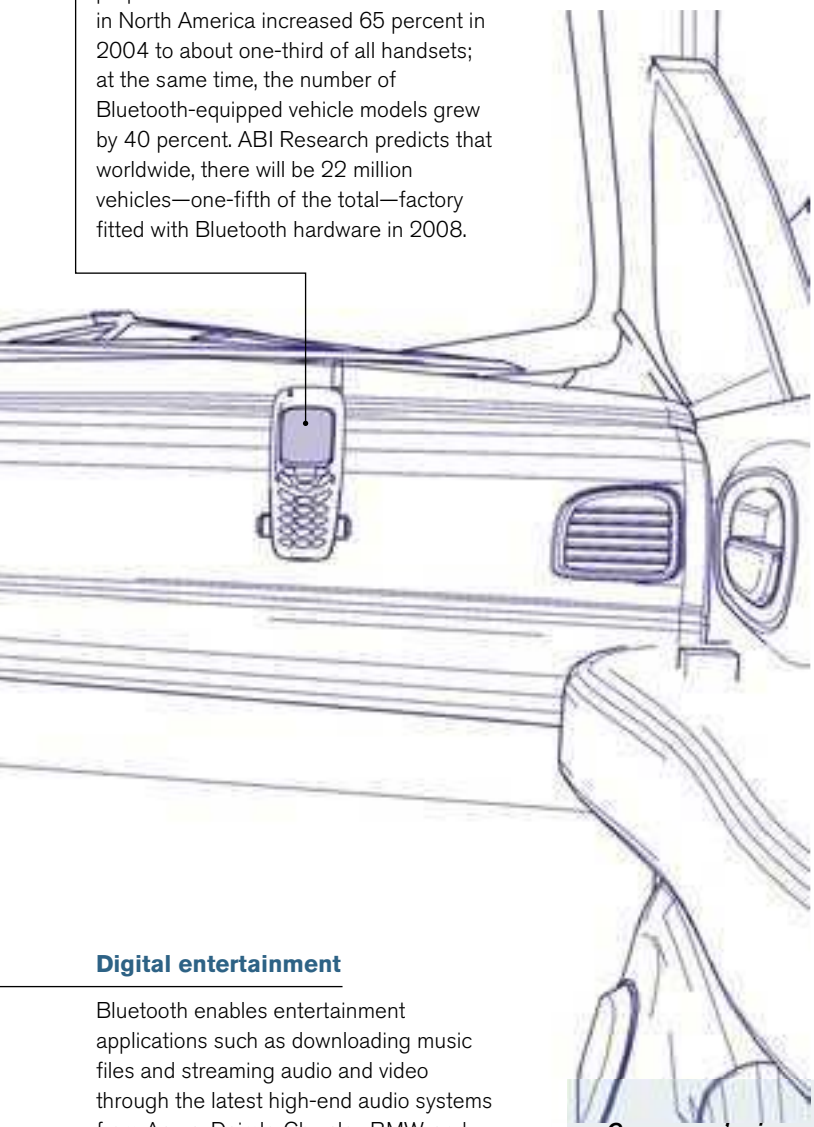
Dynamic navigation

The first service that GPS-based telematics companies like GM-backed OnStar offered was driving directions based on a car's location. This hasn't proven popular with consumers, who often let service subscriptions lapse. More likely to pique their interest is dynamic navigation, which provides directions that take into account current traffic conditions. Two 2005 models have this feature, Honda's Acura RL and GM's Cadillac CTS.

JOHN MACNEILL

Mobile networking

Telematics services could face competition from mobile phones on a variety of fronts, including communication, Internet access, and location-based services. Consequently, some automakers plan to equip their cars with Bluetooth wireless connections or docking stations so that they can network with phones. The proportion of Bluetooth-enabled handsets in North America increased 65 percent in 2004 to about one-third of all handsets; at the same time, the number of Bluetooth-equipped vehicle models grew by 40 percent. ABI Research predicts that worldwide, there will be 22 million vehicles—one-fifth of the total—factory fitted with Bluetooth hardware in 2008.

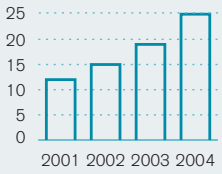


Digital entertainment

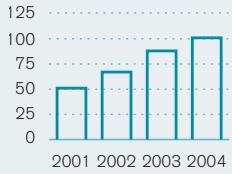
Bluetooth enables entertainment applications such as downloading music files and streaming audio and video through the latest high-end audio systems from Acura, DaimlerChrysler, BMW, and Toyota. BMW is also offering an interface with the Apple iPod. And to encourage the after-sale integration of such capabilities, the Consumer Electronics Association adopted the in-vehicle networking standard MOST (Media Oriented Systems Transport) in 2004.

Telematics by the Numbers

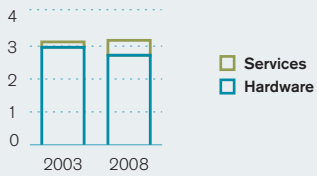
Vehicle manufacturers offering telematics



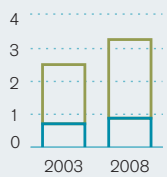
Vehicle models with telematics



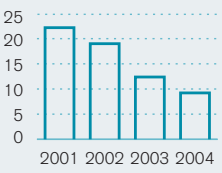
Global consumer telematics revenue (in billions of dollars)



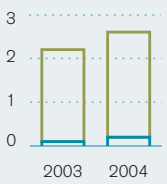
Global commercial telematics revenue (in billions of dollars)



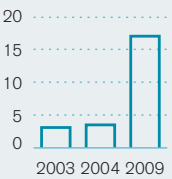
Average price of an in-car telematics system (in hundreds of dollars)



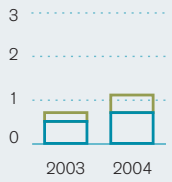
North American telematics shipments (in millions)



North American telematics subscribers (in millions)



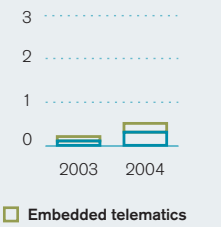
Western European telematics shipments (in millions)



Consumers' primary reason for buying telematics (according to a survey of vendors)

Safety/security services	58%
Navigation services	19%
Mobile commerce applications	7%
Communication services	6%
Vehicle diagnostics/auto maintenance services	4%
Productivity applications (e-mail, phone book)	3%
Entertainment	3%

Asia Pacific telematics shipments (in millions)



SOURCES: ALLIED BUSINESS INTELLIGENCE, EMARKETER, ABI RESEARCH, BUSINESS COMMUNICATIONS COMPANY, TELEMATICS RESEARCH GROUP

The Power of 3G = ROI

Third-generation (3G) wireless empowers members of your mobile workforce with wireless connectivity. This means road warriors can log in securely to the company VPN, check and send email, search the Internet for information or download complex documents. For your company, wireless connectivity results in streamlined processes, increased efficiencies and improved customer relationships.

Contact your wireless operator today to learn how 3G can strengthen your mobile business solutions.

For more information about QUALCOMM, visit **www.qualcomm.com**
For more information about 3G wireless, visit **www.3gtoday.com**

QUALCOMM®

Amazon: Giving Away the Store

Sometimes it makes sense to share your core assets.

Visit Amazon Light at www.kokogiak.com/amazon4, and you'll see a plain search box that allows you to locate any product in Amazon.com's database. Click on an item, and you'll be taken to a page with the usual product image, price information, and customer reviews, and, of course, the familiar "Buy This" button. Amazon Light's pages are deliberately less cluttered than those at Amazon itself, but the family relationship is obvious.

Look closer, however, and you'll spot some distinctly non-Amazonian features. If the item you're viewing is a DVD, for example, there will be a button that lets you see in a single click whether the same disc is for rent at Netflix. If it's a CD, you can check whether Apple's iTunes music store has a downloadable version. And if it's a book, Amazon Light will even tell you whether it's on the shelf at your local public library.

What's going on here? Surely, executives at Seattle-based Amazon would never condone an online service that encourages people to buy things from sites *other* than Amazon?

Actually, they would. Amazon Light, created by former Amazon programmer Alan Taylor and hosted on his personal website, kokogiak.com, is one of thousands of independent sites incorporating the product data and programming tools that Amazon has been sharing freely since July 16, 2002. That's the day Amazon celebrated its seventh anniversary—and unveiled a startling new project, called Amazon Web Services, that promises to change, once again, the way retailers of all stripes think about reaching their customers.

While companies such as Google and Microsoft are also experimenting with the idea of letting outsiders tap into their databases and use their content in unpredictable ways *(see "What's Next for Google?" p. 38)*, none is proceeding more aggressively than Amazon. The company has, in essence, outsourced much of its R&D, and a growing portion of its actual sales, to an army of thousands of software developers, who apparently enjoy nothing more than finding creative new ways to give Web surfers access to Amazon merchandise—and earning a few bucks in the process.

Amazon is "extremely aggressive" about Web services, says Paul Bausch. "They really believe that this is where their business is heading."

The result: a syndicate of mini-Amazons operating at very little cost to Amazon itself and capturing customers who might otherwise have gone elsewhere. It's as if Starbucks were to recruit 50,000 of its most loyal caffeine addicts to strap urns of coffee to their backs each morning and, for a small commission, spend the day dispensing the elixir to their officemates.

"Amazon is pouring so many resources into their Web services that it's almost frightening," says Paul Bausch, one of the inventors of the well-known weblogging tool Blogger and, more recently, the author of O'Reilly Media's *Amazon Hacks*, a collection of tips for tapping into Amazon's rich database. "They are extremely aggressive, and that separates them from Google and from other people who are still just experimenting with the technology. They really believe that this is where their business is heading."

Making the Web Safe for Computers

The strategy behind Amazon Web Services is to give programmers virtually unlimited access to the very foundation of Amazon's business—its product database—whether they are inside or outside the company's walls. Developers can grab product data, reformat it, add related services, and use it to attract eyeballs to their own sites. If they feel like it, they're even free, like Taylor, to create parallel-universe Amazons that have the added features they crave. Amazon demands only one thing in return: that visitors to these satellite sites complete any purchases through Amazon.com itself. The site owners, meanwhile, earn a decent commission on each sale.

Exposing the world's largest product database—along with the editorial content and personalization functions that make Amazon.com so uncannily useful—is such a counterintuitive business strategy* that analogies are hard to come by. In a way, the risk the company is taking is like the one Apple Computer has always avoided by refusing to license its Macintosh operating system to other manufacturers. Some observers still think Apple missed its golden opportunity to mount a comeback against Microsoft, while others maintain that the Mac OS *is* Apple, and that putting it on other machines would have diluted the brand. In Amazon's case, outside programmers could find cleverer ways of using Amazon's data than Amazon itself and end up sucking away so much traffic that Amazon's own site cedes e-retailing's center stage.

And yet Amazon's move also reflects the spirit of the age—or at least, the spirit among the Web's technical avant-garde. As Amazon CEO Jeff Bezos put it in a speech at October's Web 2.0 conference in San Francisco, "Web 1.0 was making the Internet for people; Web 2.0 is making the Internet better for computers."

Web services, whose name became a marketing meme years before the technology to make them work had actually matured, boil down to the simple but power-

* **WWW.TECHNOLOGYREVIEW.COM** Does running an open-source store make sense? Retailing experts weigh in; keyword **amazon**.

ful idea that the Web should be more than just a way for human users to call up preformatted documents. It can also be a medium for software programs to communicate and share data with one another. Through a nonproprietary formatting scheme called the Extensible Markup Language, or XML, a string of data can be labeled according to type—as, say, a phone number, a price, or a book title. Web software can then harvest the data from a remote site and re-present it to the end user in any way a programmer wishes. That means a company with a trove of data it wants to share need only put it on the public Web and give programmers a few simple tools for accessing it.

Though these tools have a geeky and daunting name—"application programming interfaces," or APIs—their function is easy to understand: they are short hooks of computer code that allow smaller programs to communicate with large software systems, such as Microsoft Windows. In the case of Web services, an API amounts to a set of commands programmers can use to interact with large, database-driven Web sites.

For a company that makes its APIs public, the real trick is figuring out how it will be rewarded. And in this respect, too, Amazon has done exceedingly well, signing up thousands of programmers who are sending it millions of hits a day, though the company won't disclose how much it's earning through their satellite sites.

There isn't one tutelary genius responsible for Web services' ascent at Amazon. Even Bezos was reportedly awakened to their possibilities only after a bit of prodding from friendly outsiders.

Rather, this is a tale of clever Amazon software engineers and marketing professionals who were attuned to emerging technologies like XML, the Simple Object Access Protocol (SOAP), and the Semantic Web, and who saw how their efforts in the 1990s to increase Amazon.com's accessibility led inexorably to the Web services model. Increasingly, it's also the tale of tens of thousands of outside Web developers with a fixation on new technologies and an urge—with Amazon's blessing—to see just how far they can stretch that model.

Amazon Everywhere

Selected sites and businesses putting Amazon Web Services to creative use

Name	*URL*	*Basic service*	*Amazon Web Services features*
Grokker	www.grokker.com	Displays search results in graphical form	Searches that use the Amazon plug-in organize products into intuitive categories
iPilot	www.ipilot.net	Key chain–sized scanner stores 100 bar codes	Codes can be used to retrieve Amazon product information for price comparisons
Monsoon	www.monsoonretail.com	Inventory management for small online retailers	Software monitors items' current Amazon prices to allow real-time competitive pricing
Naturally Open	www.naturallyopen.com	Web searches initiated by highlighting text	Browser plug-in opens a special pane listing Amazon products related to highlighted text
Yes	www.yes.net	Gives hourly playlists for 2,300 radio stations	Results include links to Amazon product pages for the corresponding music CDs

Amazon CEO Jeff Bezos

ANDY ROGERS/AP PHOTO

Amazon.com

Headquarters: Seattle, WA
Net sales, Q3 2004: $1.46 billion
Net sales, Q3 2003: $1.13 billion

The case: The company is opening its product information and computer software to outside programmers in the hope of becoming a global e-commerce syndicate—and flouting fears that it's giving away too much.

The Information Hub

There are two versions of the story of Amazon Web Services' genesis. One is told by Tim O'Reilly, a revered futurist and CEO of the software-manual publisher O'Reilly Media in Sebastopol, CA. O'Reilly says he began touting the idea of Web services as early as 2000 but wasn't seeing it blossom into the next-generation Internet programming language he envisioned. "I went up to see Jeff Bezos with a Web services pitch," O'Reilly wrote in his weblog in July 2002. "Amazon isn't just an e-commerce-site. It's become the information hub of the publishing industry. How about giving us some tools for building out services based on that hub?" Once O'Reilly enumerated the ways Amazon itself would benefit, he says, Bezos became intrigued. Bezos then "told me a day or two later that he'd discovered that his skunk-works team already had a Web services API in the works. But he says that without my presentation he 'might have done something stupid like shutting the project down.'"

Naturally, Amazon software engineers tell a different story. Robert Frederick, a 31-year-old senior technical manager at Amazon, was part of the skunk-works team that Bezos consulted after his meeting with O'Reilly. Frederick dates the origins of the project all the way back to his hiring in 1999, when he was assigned to figure out how the rich information on Amazon's website could be simplified and translated for display on the tiny screens of devices such as cell phones, PDAs, and pagers. These devices used an alphabet soup of different display formats, such as WML, CHTML, and XHTML. "To expose this information in varying markup languages was extremely challenging, given the infrastructure that [Amazon had] put in place," says Frederick. But his team eventually came up with special Web server software that could retrieve product data and reformat it for a few select devices such as the Palm VII, one of the first wireless organizers.

This project, dubbed Amazon Anywhere, succeeded so well that Frederick's bosses asked him to equip Amazon's entire battalion of Web servers with the software, the better to help partners present Amazon data in more ways. "In order to do this," Frederick says, "I advocated the separa-

tion of display logic from our business logic." More geek-speak—but that insight was perhaps the key to Amazon Web Services. It meant that Amazon needed to stop viewing its website as one giant application capable of storing product information, managing user accounts, sending product details to customers' Web browsers, processing purchases, and the like. Rather, Frederick said, Amazon.com should be reconceived as a set of independent parts, including the database, shared APIs for accessing it and repackaging the data in XML format, and the final layout as displayed in browsers. In a series of meetings with senior managers in 2001 and early 2002, Frederick argued that the more these things were separated, the easier it would be for Amazon's partners to build their own online storefronts that would draw on the Amazon infrastructure.

A few Amazon managers reacted cautiously. But "the funny thing is that it did not take a great deal of convincing," recalls Frederick. "The main concern was that we were going to expose valuable information and concepts that we had spent years developing." Absolutely true. But Frederick and his supporters argued that Amazon's payback would be the innovative applications dreamed up by external developers. In theory, these applications would vastly increase the variety of contexts in which Web surfers might encounter products from Amazon.

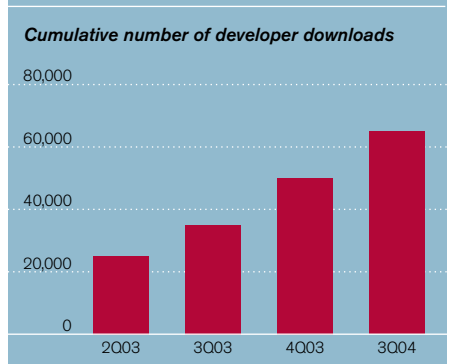
"Once we had incorporated XML, we realized that 'Wow, the future is here. We are the first to do this,'" says Jeff Barr, program manager for Amazon Web Services. "So we decided to formalize it and invite the world's developers to take a look, understand what it was all about, and start creating and innovating."

Pizzazz—and Profits

Developers accepted the invitation, and downloaded Amazon's Web services APIs, help manuals, and sample code in droves *(see "Developing Interest," above)*. "I was amazed that they did what they did, because companies are usually so reluctant to expose their databases," says Paul Bausch, who had become interested in Web services while building Blogger at San Francisco–based Pyra Labs. After Google acquired Pyra in 2003, Bausch returned to the life of an independent software developer and had so much fun playing with

Developing Interest

The number of independent software developers who have downloaded Web services tools from Amazon has more than doubled in a little over a year.



SOURCE: AMAZON.COM

Amazon's new programming interfaces that he ended up writing *Amazon Hacks*. Among other things, the book teaches readers how to embed Amazon product information in their Web pages and (on a less serious note) how to add pizzazz to their personal archives of MP3 songs by grabbing CD cover art from Amazon.

In one way, Amazon Web Services is simply an extension of longstanding collaborations such as Amazon Associates, in which external website owners can earn commissions of up to 10.5 percent for referrals. But previously, affiliate sites could only show simple links to Amazon products; with Web services, the possibilities became much broader *(see "Amazon Everywhere," p. 29)*.

At one end of the spectrum are sites like Taylor's Amazon Light that simply proffer Amazon in a different skin. At the other end are noncommercial sites where Amazon data isn't the main attraction but is used to enhance other offerings. One example is AllConsuming.net, which appeals to bibliophiles by scouring thousands of blogs every hour, listing the most talked-about books, and providing snippets from each blogger's comments. Designed by Erik Benson, another ex-Amazonian, the site dips into the Amazon database for cover images and other details about the listed books and offers links to each book's page at Amazon.

Benson says AllConsuming isn't making him rich, but it does bring in enough commissions to cover its own hardware and bandwidth costs (about $400 a month). Other companies earn far more by acting as middlemen. Monsoon of Portland, OR, for example, builds software that helps its own customers use Amazon's Web services to simplify inventory management.

By November 2004, the number of developers participating in Amazon Web Services had grown to 65,000. To keep up with their demands, the company has kept updating its APIs to open up more types of product information and more functions, such as wish lists and advanced searches. How many purchases originate each day with Amazon's growing web of syndicated storefronts? The company won't say, but experts have estimated that sites using the company's Web services send 10 million requests a day to Amazon's servers.

Amazon is far from the only company exploring Web services. IBM, for example, has opened its Websphere server software to outside developers and expects to invest $1 billion this year in new business-to-business Web services, according to Michael Liebow, director of Web services for IBM Global Services, the company's consulting wing. One IBM creation: a system that uses XML and other standards to tie together the disparate databases used by merchants, banks, and credit-card firms, helping to resolve disputed credit-card charges faster.

In fact, Web services' biggest impact may not be the syndication of individual businesses' information, as in Amazon's case, but the standardization of business processes across whole industries, such as finance, electronics, or automobiles, according to Liebow. "Amazon is unique," he says. "It's kind of a closed system, and there's a level of control."

That's true—and Amazon reserves the right to shut down its Web services at any time. But doing so would destroy the rare symbiosis that has emerged from years of careful community building. "Developers are another kind of customer for us," says Jeff Barr. "The work they do is going to bring even more diverse types of customers." In other words, by sharing not just its data but also its retailing tools and a modest slice of the profits, Amazon has turned a programming subculture typically ruled by anticorporate suspicion and paranoia into a wellspring of evangelism, not to mention a funnel for revenue. Surely, that's one for the books. **WADE ROUSH**

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Military Vaccine Studies: On Trial

Critics say the U.S. military is wasting millions on a doomed AIDS-vaccine trial in Thailand.

THIRTY-EIGHT million people around the globe are infected with HIV, and 8,000 of them die each day from AIDS. Although anti-HIV drugs can extend lives, they have serious limitations, and the vast majority of infected people still do not have access to them. So it is hard to overstate the need for an AIDS vaccine that can slow the virus's spread and ultimately safeguard the world's population.

Scientists in academia, government, and the pharmaceutical industry have spent the last 18 years testing three dozen different AIDS vaccines in human studies. Time and again, high hopes have given way to crushing disappointments, and the field has been roiled repeatedly by bitter disputes about the best way to move forward. If the different players worked in isolation, as private companies often do, the tensions might not matter much. But in the world of international vaccine research, there's a constant tussle for resources and influence among government agencies, universities, drug companies, health ministries, networks of clinics, and the communities that agree to participate.

Keeping this tussle from devolving into self-defeating conflict depends on consultation and coördination among all parties. But that's easier said than done, as was dramatically illustrated by an AIDS-vaccine trial launched in Thailand in 2004 with U.S. government backing. The study—the largest, most expensive AIDS vaccine trial in history—has turned out to be a model of bad communication, scientific disagreement, international face-saving, and clashing bureaucratic interests. Many leading AIDS researchers have publicly decried the trial as a near-certain failure and a waste of scarce resources.

The trial combines two different vaccines, and although critics don't particularly like either of them, they dislike one more than the other—and that has become the main point of contention. The controversial vaccine, called gp120, was once the darling of the field, but it fell out of favor more than a decade ago, after disappointing test results. It survives because indefatigable corporate and government scientists have brought it back time and again, arguing that it deserves yet another study to assess its worth. General scientific opinion would have dictated otherwise.

The later scientific objections surface, the more they hurt—a truth that seems to have escaped the U.S. Defense Department.

The saga began in the summer of 1993, when a protein called gp120 enjoyed frontrunner status in a spirited race to develop an AIDS vaccine. The protein sticks out from the surface of the HIV virus like the hooks in Velcro, allowing it to latch onto and infect human cells. Biotech stars Genentech and Chiron believed that injecting the surface protein into people would stimulate their immune systems to create antibodies against it, theoretically protecting them if they contracted the virus. The U.S. National Institutes of Health (NIH) planned to bankroll efficacy trials.

Then gp120's fate suddenly turned. In test-tube experiments reported in October 1993, antibodies taken from vaccinated people proved unable to stop HIV from infecting human cells. After consulting widely with critics of the approach, NIH decided in June 1994 to abandon plans for the multimillion-dollar efficacy trials.

The decision spelled the end of the gp120 programs at both companies, but out of the ashes of the Genentech effort rose VaxGen, which raised millions of private dollars to stage two new efficacy trials. Though no less a personage than Nobel laureate David Baltimore, who in 1998 headed NIH's AIDS Vaccine Research Committee, expressed serious doubts about gp120's utility, VaxGen charged that its critics put too much faith in their theories and not enough in the good old trial-and-error empiricism that had guided research on other vaccines.

As the VaxGen studies progressed, AIDS vaccine researchers moved on to the next big thing: the "prime boost." A "prime" shot would produce killer cells, which target and destroy the cells invaded by viruses, while a second "boost" shot would trigger an antibody response.

The lead candidate for the priming shot came from Aventis Pasteur, where scientists stitched HIV genes into a harmless bird virus called canarypox. For the antibody boost, researchers turned once again to gp120. Although this struck some as illogical, no other potential antibody-boosting vaccine had yet proven its safety in hundreds of humans, and gp120's proponents further reasoned that the two vaccines might somehow synergize with each other. The HIV Vaccine Trials Network, an NIH-funded group of academic researchers, and the U.S. Military HIV Research Program, run from the Walter Reed Army Institute of Research in Silver Spring, MD, drew up plans for two separate efficacy trials of the canarypox/gp120 strategy.

Backroom grumbling about these two new trials grew audible in January 2002, when AIDS immunologist John Moore of Cornell University's Weill Medical College in New York City wrote a stinging commentary for *Nature* magazine. Moore had no quarrel with the prime-boost idea, but he questioned most every other aspect of the proposed trials. Moore charged that NIH and the military behaved like rivals and felt compelled to "shadow" each other. He further argued that it "would

surely be prudent" to wait for results from the VaxGen gp120 efficacy trials then under way before launching new studies.

The next month, the HIV Vaccine Trials Network pulled the plug on its prime-boost study after small human trials of the canarypox vaccine showed that it wasn't very good at stimulating killer cells. The military, however, stood by its decision to conduct its own $119-million prime-boost study in collaboration with Thailand's Ministry of Public Health, Mahidol University, and the Thai Royal Army. In fact, the leading proponents of the Thai trial, including army colonel John McNeil, met quietly with outside consultants in Geneva in November 2002 to consider whether the design of the study should change if gp120 also failed as a solo agent. No, the group concluded, reasoning that the prime-boost strategy deserved to be tested anyway.

Predictably, the results of VaxGen's efficacy trials, released in 2003, showed that gp120 conferred no more protection against HIV than a placebo. With solid evidence that their skepticism was warranted, gp120's detractors—including Robert Gallo, whose lab first proved that HIV caused AIDS, and Neal Nathanson, the former head of the Office of AIDS Research at NIH—cranked up their objections to including the vaccine in the prime-boost study. In a *Science* magazine opinion piece published in January 2004, Gallo, Nathanson, Moore, and 19 other prominent AIDS researchers assailed the Thai trial and specifically complained about their exclusion from the Geneva meeting. The process "lacked input from independent immunologists and virologists who could have judged whether the trial was scientifically meritorious," they wrote.

McNeil and three other gp120 proponents replied in another *Science* opinion piece that the trial couldn't be stopped, since the United States had already made commitments to industry, the Thai government, and the people who had started to receive the vaccines. In a separate letter, an official at the Thai Ministry of Public Health added a revealing detail: the government of Thailand felt that the country would benefit from the study regardless of the results, since its scientists were gaining experience with HIV, its laboratories were being modernized, and general awareness of HIV/AIDS was rising.

And that, more or less, is where the controversy stands today. Last September, Thai and U.S. military scientists reported that they had enrolled more than 5,500 Thai volunteers in the study and that they would meet their goal of 16,000 participants within another year, with the entire study planned to conclude in 2009.

When scientific institutions seek robust criticism up front—as NIH did in 1994—it doesn't guarantee that everyone will walk away happy. But permitting this kind of dialogue does bow to a truth that seems to have escaped the Defense Department researchers in charge of the Thai trial: the later objections surface, the more they hurt. Had the prime-boost study's organizers invited a few well-known, sharp-edged basic researchers to take part in the study's design*, they might still have decided not to change their basic plan. But they wouldn't have had nearly two dozen leading scientists in the field publicly accusing them of playing ostrich.

Indeed, when the stakes are as high as they are in the search for an AIDS vaccine, it's worth striving to keep the peace in constituent communities, even if it means inviting your enemies to the table. But that's a battle plan that simply runs counter to the culture at the Department of Defense.

JON COHEN

Trial Period

Several preventative HIV vaccines are currently moving through the clinical-trials process.

Vaccine	*Trial phase*	*Location*	*Start date*	*Sponsors/Manufacturers*
Canarypox/ gp120	III (large-scale safety and efficacy)	Thailand	October 2003	U.S. Military HIV Research Program, U.S. National Institutes of Health, Thai Ministry of Public Health, Mahidol University, Aventis Pasteur, VaxGen
Lipopeptides	II (safety and immune responses)	France	September 2004	Agence Nationale de Recherches sur le SIDA, Aventis Pasteur
DNA/Adenovirus	II (safety and immune responses)	United States	Second quarter 2005	NIH Vaccine Research Center
Adenovirus	I/II (safety, dosing, and immune responses)	Caribbean, Southeast Asia, South America, South Africa, Malawi	September 2004	Merck, NIH
DNA/Fowlpox	I/II (safety, dosing, and immune responses)	Australia	June 2003	University of New South Wales, Australian Vaccine Consortium
Venezuelan equine encephalitis	I (safety and dosing)	United States, South Africa	July 2003	AlphaVax, NIH

SOURCE: UCSF CENTER FOR HIV INFORMATION, HIV VACCINE TRIALS NETWORK, IAVI REPORT

U.S. Military HIV Research Program

Headquarters: Rockville, MD
Budget: $21 million per year

The case: U.S. Defense Department AIDS researchers dodged open debate when they pushed forward a costly AIDS vaccine trial. This came back to bite them.

Drawing blood from a vaccine-trial volunteer.

PAULA BRONSTEIN/GETTY IMAGES

* **WWW.TECHNOLOGYREVIEW.COM** Why did the canarypox/gp120 trial become so controversial? What would be an equitable way to design vaccine trials? Experts weigh in; keyword **HIV**.

Mitsubishi: Out Front in Nanotech

Advance diplomacy may help the Japanese giant sidestep opposition to nanoparticle manufacturing.

Fullerenes, those soccer ball–shaped carbon molecules also known as "buckyballs," have generated outsized expectations ever since their discovery in 1985. Scientists think they could eventually be used in chemical sensors, fuel cells, drug delivery, cancer medicines, and smart materials. Yet while commercial demand for fullerenes is gradually emerging, so are fears that these molecules, which measure only a few billionths of a meter across, pose serious health and environmental hazards.

To some, however, fullerenes' potential is too great to ignore. Mitsubishi Corporation, which holds a number of key patents and licenses on fullerenes, began laying the groundwork for their commercialization in 1993, and company executives say they realized from the beginning that they would need to do voluntarily what many companies won't do until forced: consider the concerns of stakeholders in academia, government, the environmental community, and the public.

In 2001, Mitsubishi Corporation and Mitsubishi Chemical, one of its sister firms in the Mitsubishi group, created Frontier Carbon to manufacture fullerenes. Today Frontier produces only a small amount of fullerenes for its 350 Japanese customers. But already it can make 40 metric tons of fullerenes a year and will eventually expand that capacity to 1,500 metric tons per year. No other producer comes close to these volumes. In fact, nanotechnology industry observers say the two Mitsubishis are taking a big risk by powering up fullerene capacity before there's a market. They are, in one nanotechnology pundit's words, "putting the cart, the barn, and the farm before the horse."

And then there are the health concerns. It's well known that fullerenes suck up loosely bound electrons from neighboring molecules. Inside the body, this phenomenon releases free radicals that can wreak havoc on cell chemistry. And in a possible confirmation that fullerenes produce this effect, a highly publicized study described at an American Chemical Society meeting last March found that bass fish exposed to the molecules developed brain damage.

Counteracting such fears won't be easy, since Japan, along with most of the industrialized world, lacks a government-approved system for monitoring, testing, or certifying nanotechnology products. But thanks in part to the efforts of Mitsubishi Corporation, Mitsubishi Chemical, and Frontier, Japan is well on its way to becoming the first nation with such protections, which could help inoculate its companies against a nanotech backlash.

Frontier was acutely aware of the fate of previous attempts to introduce controversial technologies, says Hideki Murayama, vice president and general manager of the company's research and development center. For example, consumer resistance to Monsanto's plans to sell genetically modified crops in Europe in the late 1990s snowballed into a five-year EU moratorium on the approval of new genetically modified organisms. Frontier is eager to avoid similar mistakes. "We know about the health and environmental concerns," Murayama says. "We very much want to address these concerns in a collaborative way so that everybody can see that we take them very seriously and aren't trying to hide what we know and don't know about them."

In one collaboration, representatives of Mitsubishi Corporation and several other Japanese chemical companies and universities are in discussions with Japan's Ministry of Economy, Trade, and Industry over what existing regulations might also be applied to fullerenes, and what new regulations might be needed to limit people's and animals' exposure to nanomaterials.

"Murayama has made very smart moves* and kept us completely informed," says Masahiro Takemura, a nanoscale-materials specialist at Japan's National Institute for Materials Science. "At this point, he deserves our help, because he's helping Japan in a way that brings us honor, educates the public, and will probably make the companies more competitive."

It remains to be seen whether this ringing endorsement ultimately translates into sensible regulations and profits. But Mitsubishi is fortifying the trust and the relationships that it will need in the future if fullerenes are to reach their potential. It's also reminding industry that the time to address public fear and regulatory bewilderment is before the backlash, not after.

STEPHAN HERRERA

Mitsubishi Chemical

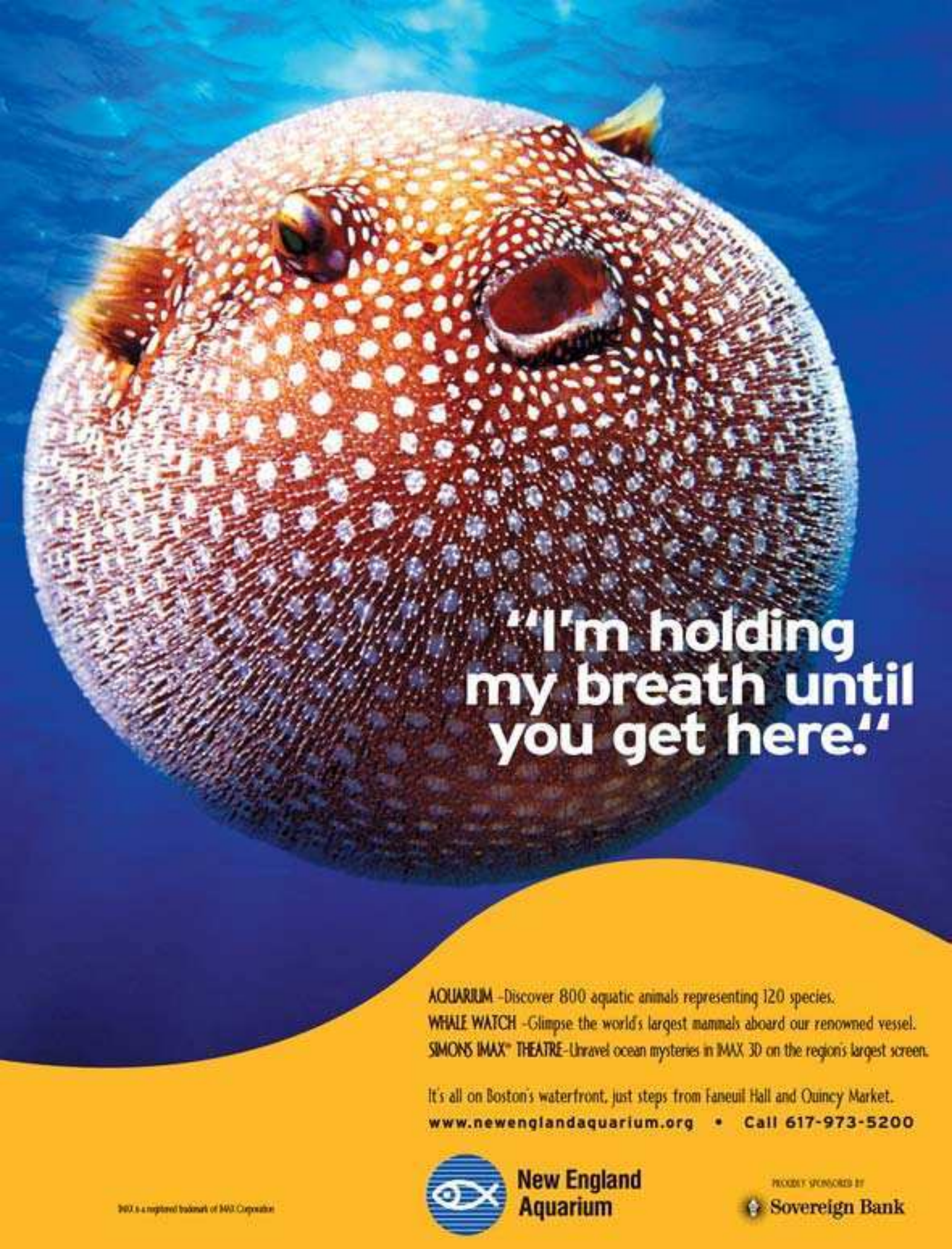
Headquarters: Tokyo, Japan
Net sales, Q1 2005: $4.61 billion
Net sales, Q1 2004: $4.28 billion

The case: To ensure that a commercial market emerges, Mitsubishi is working ahead of time to abate concerns about the health effects of the carbon molecules known as fullerenes.

Sixty carbon atoms join in a buckyball.

KENNETH EDWARD/BIOGRAFX/PHOTORESEARCHERS, INC.

* **WWW.TECHNOLOGYREVIEW.COM** When does it make sense to work proactively with government? Industry weighs in; keyword **fullerenes**.



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A New Idea for Publishing

Smart Web ads could restore balance to media

JOHN KASCHT

John Battelle is a cofounder of *Wired* magazine and was the founder of Standard Media, the publisher of The *Industry Standard*. His thoughts on media can be found at John Battelle's Searchblog (battellemedia.com).

Ideally, commercial media would consist of equal partnerships between three parties: publishers, the audience, and advertisers. In reality, advertisers, the group with the most money, hold all the cards. Publishers have been relegated to the role of supplicant, and the audience—well, we pretty much have to swallow whatever deal the publisher and the advertisers cut.

For the most part, the Internet has inherited this model from print publishing: on the Web, there are far more publishers trolling for ad dollars than there are advertisers doling them out. But the Internet's interactivity suggests an alternative economy in which the long-standing imbalance between publisher, audience, and advertiser could be corrected. A system of Internet-based marketing, which I'll call Publisher-Driven Advertising, or PDA, may be soon possible. In this system, publishers would pick and choose from a vast supply of advertisers.

The first step toward building such a system has already been taken: the pay-per-click (PPC) network. If you have ever visited Google or any content site that runs Google's ads, you've seen it *(for more on Google's advertising networks, see p. 38)*. Those text-based ads on the right side of the screen represent two shifts in the traditional relationship between publishers and advertisers. First, the advertiser pays only when the ad performs—when someone clicks on the ad itself. Second, paid search networks "disaggregate" advertisers from publishers—that is, advertisers no longer purchase space on the publisher's site but instead pay for keywords.

When PPC networks were first introduced, publishers were understandably concerned. PPC undermined what they had worked hard to build: a community of loyal readers. PPC networks claimed that those readers were only valuable if they acted—that is, clicked on an ad.

Advertisers initially loved paid search for one simple reason: it worked, driving valuable leads to their sites. But the publishers' concerns were well-founded. After all, paid search can undermine the value of a publisher-created community. It also fails to garner the benefits of a publisher's influence and endorsement. Finally, advertisers care a lot about where their ads appear. A big question arises: can we create an advertising model that has all the benefits of paid search and at the same time values the relationship between publisher and audience?

Imagine that we start with the idea of PPC—that advertisers pay publishers only if their ads are acted upon by readers. Next, imagine that, instead of buying into PPC networks or specific sites, advertisers release their ads onto the Internet.

Because an Internet-based ad is already a little piece of software, it can be tagged with information about its target audience, how much the advertiser is willing to spend to reach that audience (and how much each click will cost), what kind of websites are acceptable or forbidden (such as porn sites), and any number of other attributes. Most important, each ad could communicate with a "home" application that tracks its progress and status.

Once these tagged ads are let loose, publishers could simply copy and paste them into their own websites. Through connections to their home sites, the ads would report which publishers have pasted them where, how many clicks they've received, and how much money is left in the advertiser's bank account. The ad propagates until it runs out of money. If it is working, the advertiser simply fills up the tank with more money.

Why is this model better than the current one? Because publishers know their audiences best. There's no incentive for publishers to place ads that don't perform or that offend their readers.

How might such an idea take root? Weblogs. These "micropublishers" have credibility and influence with their online communities, and if they decided to run PDA-based advertising, it could be taken as tantamount to an endorsement of the system itself.

This adds yet another element to the PDA system: publisher influence. PDA allows publishers to declare their support of certain advertisers by deciding to run their ads. This new system of advertising might even incorporate a "cost-per-influence" metric that would reward publishers for propagating ads to other sites*.

Although there are technological and business problems that still need to be ironed out, Publisher-Driven Advertising could work, especially because it benefits all the parties involved. When PPC was first proposed, it was dismissed as a joke. Today, it's a $5 billion industry. ■

**This article was inspired by many things, but particularly by Ross Mayfield's "Cost Per Influence" post at ross.typepad.com/.*

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What's Next for Google

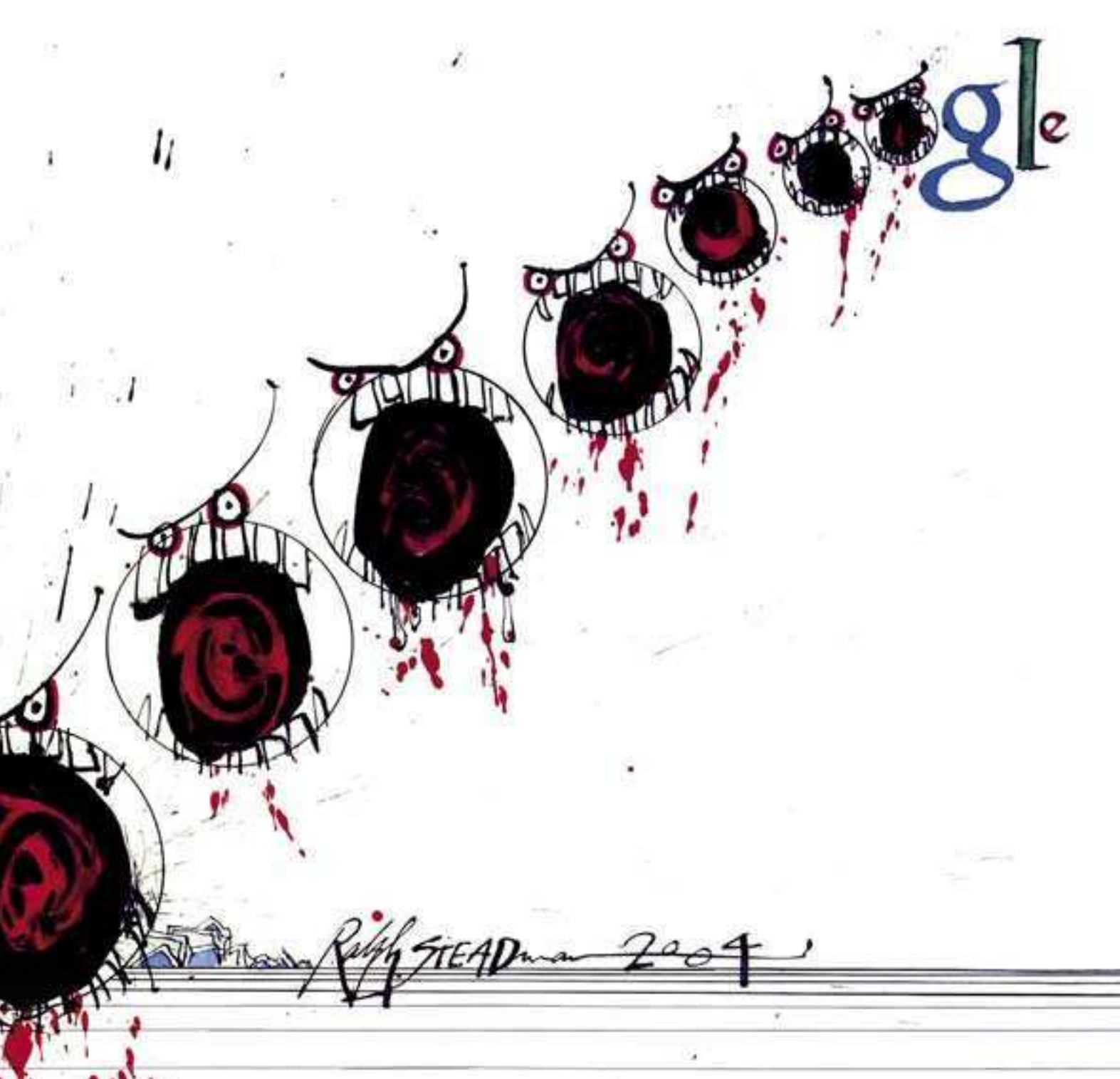
The search firm wants to organize all digital information. That means war with Microsoft.

By Charles H. Ferguson

ILLUSTRATIONS BY RALPH STEADMAN

For Eric Schmidt, Google's CEO, 2004 was a very good year. His firm led the search industry, the fastest-growing major sector in technology; it went public, raising $1.67 billion; its stock price soared; and its revenues more than doubled, to $3 billion. But as the search market ripens into something worthy of Microsoft's attention, those familiar with the software business have been wondering whether Google, apparently triumphant, is in fact headed off the cliff.

I've seen it happen before. In September 1995, I had breakfast with Jim Barksdale, then CEO of Netscape Communications, at Il Fornaio in Palo Alto, CA, a restaurant popular with Silicon Valley dealmakers. Netscape had gone public a few months earlier, and Netscape Navigator dominated the browser market. Ver-



meer Technologies, the company that Randy Forgaard and I had founded 18 months earlier, had just announced the release of FrontPage, a Windows application that let people develop their own websites. Netscape and Microsoft were both preparing to develop competing products. Our choice was to stay independent and die or sell the company to one of them.

At breakfast, and repeatedly over the following months, I tried to persuade Barksdale to take Microsoft seriously. I argued that if it was to survive, Netscape needed to imitate Microsoft's strategy: the creation and control of proprietary industry standards. Serenely, Barksdale explained that Netscape actually *invited* Microsoft to imitate its products, because they would never catch up. The Internet, he said, rewarded openness and nonproprietary standards. When I heard that, I realized that despite my reservations about the monopolist in Redmond, WA, I had little choice. Four months later, I sold my company to Microsoft for $130 million in Microsoft stock*. Four years later, Netscape was effectively dead, while Microsoft's stock had quadrupled.

Google now faces choices as fundamental as those Netscape faced in 1995. Google, whose headquarters in Mountain View, CA—familiarly called the Googleplex—is only five kilometers from Netscape's former home, needn't perish as Netscape did, but it could. Despite everything Google has—the swelling revenues, the cash from its initial public offering, the 300 million users, the brand recognition, the superbly elegant engineering—its position is in fact quite fragile. Google's site is still the best Web search service, and Gmail, its new Web-based e-mail service, Google Desktop, its desktop search tool, and Google Deskbar, its toolbar, are very cool. But that's all they are. As yet, nothing prevents the world from switching (painlessly, instantly) to Microsoft search services and software, particularly if they are integrated with the Microsoft products that people already use.

In November 2004, Microsoft launched a beta, or test, version of a search engine designed to answer questions posed in everyday language and to serve results customized to users' geographical locations. Microsoft has also created additional search software for its Internet Explorer browser and its Office productivity applications. That Microsoft is developing its own Web search engine and desktop search tools is significant in itself. But its competition with Google will have repercussions far beyond the existing search business—or even the software industry itself. Google and Microsoft will be fighting to control the organization, search, and retrieval of *all* digital information, on all types of digital devices. Collectively, these markets are much larger than the existing market for search services. Over the next several decades, in the view of search industry insiders I've spoken with, they could generate perhaps *half a trillion dollars in cumulative revenue*.

Microsoft is starting late but has extraordinary resources and powers of persistence—and it joined the browser wars late, too. In contrast, Google is youthful, adventurous, and innovative, and it does some things extremely well. The contest could end in a Cold War standoff, a decisive victory for either side, or even mutual destruction, if the competition frightens away customers and investors.

Peaceful coexistence, however, seems unlikely.

The Prize and the Contestants

Eric Schmidt and Microsoft's Bill Gates will be competing against each other for the third time. For both men, the contest is personal as well as financial.

Gates's philanthropic ambitions depend on Microsoft's continued health. And like a rock star who yearns to be admired for his brains, Gates wants to create new technology. Only by doing so can he overcome his reputation as the college dropout who built his empire by turning other people's ideas into mediocre products. "Bill Gates is desperate to prove that he can innovate," commented a Microsoft executive who prefers to remain anonymous. "And it just might kill us." He pointed to the ambitious goals and long delays that have plagued Longhorn, Microsoft's future (and search-centric) version of Windows.

By contrast, the three men who run Google have impeccable technology credentials. Schmidt has a PhD from the University of California, Berkeley, did research at Xerox PARC, and became chief technology officer of Sun Microsystems, where he oversaw the development of many impressive technologies. In business, however, Schmidt has twice been beaten by Gates. The first time was at Sun; the second was at Novell, where Schmidt was CEO. Both firms made enormous mistakes. Schmidt wasn't entirely responsible, however, because his hands were tied by his superiors at Sun and by his predecessors at Novell. At Google, Schmidt must once again share power—with Larry Page and Sergey Brin, Google's brilliant but young and possibly overconfident founders, both "on leave" from Stanford University's PhD program in computer science. Page and Brin still call many of the shots, and the company's unusual capital structure gives them about 30 percent of the voting shares.

Google seeks to become the gatekeeper for not only the public Web but also the "dark" or hidden Web of private databases, dynamically generated pages, controlled-access sites, and Web servers within organizations (estimated to be tens or even hundreds of times larger than the public Web); the data on personal computer hard drives; and the data on consumer devices ranging from PDAs to cell phones to iPods to digital cameras to TiVo players. Google's founders understand the scale of the opportunity. Larry Page recently said, "Only a fraction of the world's information is indexed on our computers. We are continually working on new ways to index more.... Thirty percent [of our engineers] are devoted to emerging businesses." And Sergey Brin once told *Technology Review*'s editor in chief, "The perfect search engine would be like the mind of God."

WWW.TECHNOLOGYREVIEW.COM For examples of Bill Gates's previous crusades against competitors, see our visual history. Keyword **microsoft**.

Until now, competition in the search industry has been limited to the Web and has been conducted algorithm by algorithm, feature by feature, and site by site. This competition has resulted in a Google and Yahoo duopoly. If nothing were to change, the growth of Microsoft's search business would only create a broader oligopoly, similar, perhaps, to those in other media markets. But the search industry will soon serve more than just a Web-based consumer market. It will also include an industrial market for enterprise software products and services, a mass market for personal productivity and communications software, and software and services for a sea of new consumer devices. Search tools will comb through not only Microsoft Office and PDF documents, but also e-mail, instant messages, music, and images; with the spread of voice recognition, Internet telephony, and broadband, it will also be possible to index and search telephone conversations, voice mail, and video files.

All these new search products and services will have to work with each other and with many other systems. This, in turn, will require standards.

The emergence of search standards would encourage tremendous growth and provide many benefits to users. But standardization would also introduce a new and destabilizing force into the industry. Instead of competing through incremental improvements in the quality and range of their search services, Microsoft, Google, and Yahoo will be forced into a winner-take-all competition for control of industry standards. Steve Jurvetson, a venture capitalist at the firm of Draper Fisher Jurvetson in Menlo Park, CA, says, "This is something of a holy war for Microsoft*, and one they can't bear to lose."

In short, the search industry is ready for an architecture war.

Size of the Prize

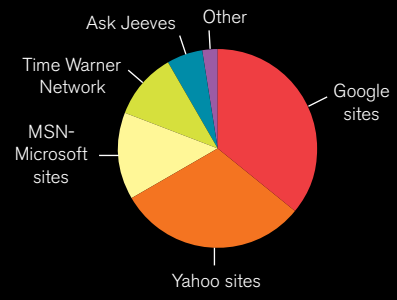
The searchable Internet (in red) contains only a fraction as much information as the various other forms of digital media.

Media type	Terabytes	Unique items per year
Newsletters	1	40,000 titles
CD-ROMs	1	850 titles
Scholarly periodicals	6	37,609 titles
Books	39	950,000 titles
DVD videos	44	4,000 titles
Mass-market periodicals	52	80,000 titles
Audio CDs	58	33,443 titles
Newspapers	138	25,276 titles
Searchable Web	167	
Instant messaging	274	
Zip disks	350	1.4 million
Floppy disks	800	55 million
Office documents	1,397	10.75 billion pages
Audio MiniDisks	1,700	10.5 million
Flash memory	2,200	43 million
X-rays	20,000	2 billion
Motion pictures	25,000	10,342
Deep Web	91,850	
Audio tapes (analog)	128,800	128.8 million
Digital tapes	250,000	5 million
Photographs	375,000	75 billion
E-mails (originals)	440,606	
Digital video	1,265,000	115 million
Video tape (VHS and camcorder)	1,340,000	220 million
Hard disk drives	1,986,000	44 million

SOURCE: HOW MUCH INFORMATION? 2003

Feeling Lucky

Google's own sites perform 36 percent of Web searches. Sites that license its technology account for another 10 to 15 percent.



DATA AS OF AUGUST 2004. SOURCE: COMSCORE MEDIA METRIX

Pursuing Lock-In

Architecture wars (also known as standards wars) occur because information technology markets require standards in order to manage complexity, communication, and technological change. Historically, proprietary control over a major information technology standard has created more wealth than nearly any other human activity. Architectural dominance *mints* money; and managed properly, it lasts forever. IBM's mainframe architecture was introduced in 1964; Intel developed its first microprocessor in 1971; Microsoft's first operating system was introduced in 1981; Cisco Systems marketed its first router in 1986. None shows any signs of disappearing, and each has already generated hundreds of billions of dollars in cumulative revenues.

It is only standardization that makes it possible for any browser to display any Web page, or for people to read the documents and e-mail messages they receive from each other. Standards are generally based upon the *interfaces* that constitute the authorized ways for software systems to communicate with each other. These include *application programming interfaces*, or APIs, like those Microsoft provides for developing Windows applications; *communications protocols* such as HTTP (the hypertext transfer protocol), which allows browsers to communicate with websites; and *content* or *document structures*, such as the HTML (hypertext markup language) standard for Web pages, or the document structure used by Microsoft Word. These standards are embedded in larger *architectures* used in the design of general-purpose commercial systems, or *platforms*, such as the Windows operating system. Platforms, in turn, are used as the starting point for specific applications, such as word processors or accounting systems.

Sometimes standardization is achieved through nonproprietary efforts managed by governments, standards bodies, or industry coalitions. Examples include the basic Internet protocols, the HDTV broadcasting standard, and most telephone standards. In other cases, like that of the Ethernet protocol invented by Bob Metcalfe while at Xerox PARC, a company donates an architecture to a standards body in the hope of creating or expanding a market. The open-source movement is an interesting variant of nonproprietary standardization based on decentralized control. In the case of open-source software like the Linux operating system, a community of creators and users in effect votes continuously on the direction of a standard.

But in most information technology markets, standardization is achieved via market competition. These contests are extremely complex, but they have a common underlying logic, which Charles Morris and I described a decade ago in our book *Computer Wars*. The best technology does not always win; superior strategy is often more important. Winners do tend, however, to share several important characteristics. They provide general-purpose, hardware-independent architectures, like Microsoft's operating systems, rather than bundled hardware and software, like Apple's and Sun's systems. Winning architectures are proprietary and difficult to clone, but they are also externally "open"—that is, they provide publicly accessible interfaces upon which a wide variety of applications can be constructed by independent vendors and users. In this way, an architecture reaches all markets, and also creates "lock-in"—meaning that users become captive to it, unable to switch to rival systems without great pain and expense.

Architecture wars generally begin with a fierce competition for market share. Eventually, the market settles on a de facto standard, a dominant architecture under the proprietary control of one company. Subsequently, only a few rivals survive in the leader's shadow, while the leader expands its empire into neighboring markets.

The search industry is the next place in which a vast architectural empire could be built. Some portions of the emerging search space are now occupied by Google, others by Microsoft, most by nobody. But in the end, there will probably be room for just one architecture. Google's idyllic childhood must therefore give way to a contest much like those Microsoft has fought and won against companies ranging from IBM to Novell to Apple to Netscape. But for several reasons, this architecture war may end differently. First, many of the companies defeated by Microsoft over the past 20 years suffered as much from self-inflicted wounds as from Microsoft's predation. In Eric Schmidt, Google may have a CEO with the technological depth and painfully acquired experience

essential to surviving Bill Gates. Second, Google's principal services run on a platform that Microsoft doesn't control—the Web. Third, in some cases (like its fight against Linux, for example), Microsoft's software is now the high-cost incumbent.

Fourth, some analysts believe that Microsoft has lost its edge, that its size and age have bred complacency. Commenting on the collision between Google and Microsoft, Internet industry observer John Battelle recently wrote, "Microsoft is indeed a fearsome competitor, with extraordinary resources (and I don't mean the $50 billion in cash; I mean the ability to leverage Windows). But it's a middle-aged company that moves far more slowly than it did ten years ago, when it first recognized the Web threat." *(For John Battelle's views on the future of publishing, see "Megaphone," p. 36.)*

Fifth, Microsoft hasn't always won: Adobe and Intuit are doing just fine, MSN hasn't killed AOL or Yahoo, and the Xbox hasn't defeated the Japanese game industry (not yet, anyway). And finally, Microsoft's recent entry in the search wars—the beta version of MSN's search tool—is decidedly unimpressive. (Then again, Windows 1.0 was pretty bad, too.)

So Google's defeat is not a foregone conclusion. Indeed, if it does everything right, it could become an enormously powerful and profitable company, representing the most serious challenge Microsoft has faced since the Apple Macintosh. But if Microsoft gets serious about search—and there is every reason to believe that it will—Google will need brilliant strategy and flawless execution simply to survive.

Arming Secretly

Does Google understand the gravity of the challenges that may confront it? Does it have a strategy for winning an architectural war? The evidence is equivocal.

Google has software developers skilled enough to construct a powerful architectural position. It has hired both newly minted PhDs and experienced technologists from Netscape and even Microsoft. One of its newer employees is Adam Bosworth, famous to software developers for developing the HTML engine in Microsoft's Internet Explorer and for his pioneering work on the Extensible Markup Language, or XML, the standard for machine-to-machine communication on the Web. Other recent hires, significant for their architectural expertise, include Rob Pike, a pioneer of the Unix operating system at Bell Labs; Joshua Bloch, a leading Java coder from Sun; and Cédric Beust, who developed the Weblogic platform at BEA Systems.

One Google manager, who preferred not to be named, said his company understands the need for proprietary control, and that future products would prove it. In late 2004, Google did release two important new APIs, for its Deskbar search tool and its advertising systems. But the Google executive declined to comment on

future plans, noting that his employer had become secretive to the point of paranoia. (Indeed, Google's senior executives refused to be interviewed for this article.)

The executive then went on to say, "Look, everyone here—right up to our CEO and board of directors—has had the shit kicked out of them over the last five years. A lot of them were at Netscape, or at failed dot coms. Nobody I work with is complacent, and they're all very smart." But there are two important people who haven't had the shit kicked out of them: Google's founders. In a *Playboy* interview published shortly before Google's IPO, Brin and Page did not mention competitive threats. Rather, they talked about corporate ethics, the creation of foundations, and their efforts to make Google a great place to work.

Google is a great place to work. My friends there absolutely love the place, and in part for that reason, they work very hard. Google allows pets and provides employees with laundry service, drinks, meals, massages, car washes, and (soon) child care. Its corporate motto is "Don't be evil." But long ago, a professor of mine, noting my youthful idealism, remarked that the only successful neutral nations are those, like Switzerland, that are permanently armed to the teeth. And for Google, neutrality is not an option.

But what specifically should Google do? How is Microsoft likely to attack, what will the contest look like, and what will decide its outcome? Let's begin with the current state of search.

The State of Search

For a long time, search engines were expensive luxuries for those who operated them. They never made money. Market leadership traded hands repeatedly. Sites like AltaVista rose to prominence and fell away. The entirely separate business of selling software products for text indexing and retrieval was a backwater. But then things changed. As the Internet and the Web grew, searchable digital content began to supplant conventional media, and efforts to improve the quality of search results intensified.

Early search engines ranked results largely according to crude criteria such as the number of times a page mentioned the user's chosen keywords. But in a research collaboration that began in 1995, when they were still graduate students, Brin and Page applied a practice called citation ranking to the Web, and it turned out to be a much more reliable way to find relevant information.

For many years, reference publications like the *Science Citation Index* have ranked scientific papers' "impact" by counting the number of times they were cited in other papers. Brin and Page's insight was that if hyperlinks were viewed as citations, the same thing could be done for the Web. That insight led to the first truly superior search engine. Stanford applied for a patent on Brin and Page's "PageRank" technique in 1998 (it was granted in 2001). Soon afterward, Brin and Page started Google and raised money from top-tier venture capital firms Sequoia Capital and Kleiner, Perkins, Caufield, and Byers.

Today, the search industry has two layers. The leaders, Google and Yahoo, both provide "retail" search services on their own websites. But both firms also license, on a highly selective basis, their infrastructure and services to other companies in a "wholesale" market. For example, Google provides the underlying search services for AOL and Amazon.com's A9 search subsidiary. Looksmart powered MSN Search for some years. Now, however, Microsoft is developing its own search engine.

Google holds nearly 40 percent of the U.S. retail search market, more than 50 percent of the U.S. wholesale market, and larger shares of the global market. Yahoo enjoys a rough parity with Google in the United States, and Baidu has been expanding in China. Interestingly, while Google operates its own service in China, it also holds an equity stake in Baidu.

Google derives nearly all of its revenues from advertising, of two distinct kinds. First, it places advertisements on pages of search results returned by its own site. Those advertisements are selected according to the words used in the search. Advertisers bid in highly complex auctions for the right to place ads on results pages for searches that use specific terms like "used cars," "SUVs," and so forth. Second, Google manages advertising for a wide network of external websites for which it provides ad placement services. It has combined its search engine with sophisticated text-matching and auction systems to target, price, sell, and evaluate its advertisements, both those placed on its own site and those on its affiliates'.

Some of these affiliates use Google's search services, but most do not. In fact, almost half of Google's revenue and profits come from its external advertising network, a business where its superior indexing and search capabilities play a less critical role. Google also sells a "search appliance," a Linux server running its indexing and search software, to organizations wishing to provide search services for their internal Web servers. This business, however, is quite small.

Yahoo's search business is similar. Like Google, Yahoo earns a substantial fraction of its total revenue through search-related advertising, both on its own site and on a network of affiliates. Yahoo's portal offers a wider variety of information services than Google, including news, dating, chat, and shopping. But Google is rapidly diversifying: in addition to allowing users to download its free personal search tool, Google's website has news, shopping, e-mail, and photo storage services in various stages of development.

Today, the wholesale search market has significant barriers to entry. Economies of scale have asserted themselves, secondary competitors have folded, and the creation of new search engines by startups is becoming prohibitively expensive. Consider: to crawl, index, and search more than eight billion pages—still only a fraction of the Web—Google now operates a global infrastructure of more than 250,000 Linux-based servers of its own design, according to one Google executive I spoke with, and it is becoming a major consumer of electrical power, computer hardware, and telecommunications bandwidth.

But the consolidation of the wholesale market does not mean that the search industry is mature. Quite the contrary.

First, there is no lack of new competition. This comes from any number of sources: large firms, like Amazon and its A9 subsidiary, with sufficient resources to enter the market; startups commercializing a wide variety of new search functions; information retrieval and filtering firms such as LexisNexis or Vivísimo, whose products are competitive with or complementary to Web-based search services; and, in a class by itself, Microsoft. Moreover, while basic Web crawling is a mature technology with high barriers to entry, many other search-related functions are not. Secondly, services that have thus far been confined almost exclusively

to the public Web are now expanding to personal computers, the dark Web, and other platforms. Finally, the search arena is still unstructured and without standards. Search sites are self-contained islands. They do not interoperate, and independent developers cannot use search sites as platforms upon which to offer specialized products and services, because, with minor exceptions, the search industry lacks open APIs. For the most part, each service is confined to what it can do on its own.

But the search industry cannot resist APIs, standards, and open architectures much longer. No single company can offer users all the functions they want. Users will demand search products and services that work across many different platforms. And Microsoft will almost certainly exploit both its ownership of the Windows platform and its search engine. Indeed, Microsoft has already announced that it intends to provide third-party developers with APIs to its new search engine, enabling them to construct applications based on it.

Trends in Search: Technology

The advantage conferred on Google by its PageRank algorithm, once overwhelming, is gradually disappearing. Many other clever algorithms have been developed; indexing and searching are being applied to more data sources and data types; and ever more nuanced user interfaces and functions are being offered to users.

Some of these efforts seem quite promising. Amazon has scanned more than 100,000 books and made their text searchable for Amazon users. Google Print provides a similar service and also offers direct links to bookselling sites. PubSub, a small startup in New York City, has developed a high-performance "matching engine" that monitors online information: if you subscribe to a topic, PubSub will scan data in real time and notify you whenever there is news. For the sorting and clustering of search results, the leader is Vivísimo, a Carnegie Mellon University spinoff in Pittsburgh, with its new Clusty website. Software from Blinkx, of San Francisco, lets users search multiple information sources, including their desktops, websites, and blogs. X1 Technologies of Pasadena, CA, also provides a popular desktop search tool.

As these examples suggest, many new search functions are being introduced by startups rather than by Google or established companies. A few of these startups may become large, independent firms. But most will remain small vendors, will be acquired, or will simply fail, depending on what Google, Yahoo, or Microsoft choose to do. Many offer products that would be natural additions or complements to existing search services, since their utility depends upon access to a search engine. But Google and Yahoo do not usually provide such access, even though it would benefit users. Google's sole Web API is laughably limited, offering little functionality and contractually restricting users to 1,000 queries per day.

Just what services could be built upon a fully open Google architecture? They could take many forms, but some of the most obvious would make indexing and searching processes on the desktop, on Web servers, and on Google's own website work together better. A single search could then span not just Google's index of the public Web but whatever other sources might be appropriate: a newspaper archive, a medical database, an antique-car parts catalogue, or your own hard drive. Google, or others building upon its APIs, would unify the results, explain any access restrictions on particular sources, and facilitate purchases of information. At the same time, independent firms could create services that call on Google's search and indexing functions to retrieve information, but present that information in new and creative ways.

As the search industry evolves, it also touches upon—and often competes with—a widening array of other industries, from publishing to software, in both business and consumer markets. The search industry wants to become the starting point for a larger proportion of digital activities. Some companies are happy to oblige: Amazon, for instance, opens its databases to search services, so that search results can point directly to relevant Amazon products, bypassing the need to navigate Amazon's own site. Others are less welcoming. Microsoft will be displeased, to put it mildly, if Google Desktop begins to supplant the traditional Windows desktop interface and file systems.

However, the most important trend in the search industry is the proliferation of new computing platforms—and the increasing cross-pollination of data between these devices, PCs, and Web services. These emerging—and merging—markets represent Google and Microsoft's greatest opportunity for future growth and the greatest threat they pose to each other. In the absence of a common architecture, the information on these systems is almost unsearchable. Today, a user cannot possibly conduct a search such as "Show me everything about the Chinese economy that has appeared in the last month in my e-mail attachments, Word documents, bookmarked websites, corporate portal, voice mail, or Bloomberg subscription." Many computing platforms, old and new, have no useful search facilities at all. Most existing search tools are available on only one or at most a few platforms; and due to their lack of standardization, they cannot talk to each other.

Thus, while Google provides an excellent service for searching the public Web and has made a good start on PCs with Google Desktop (the hard-drive search tool) and Google Deskbar (which performs searches without launching a browser), the search universe as a whole remains a mess, full of unexplored territories and mutually exclusive zones that a common architecture would unify. Given the size and growth rate of the markets involved, the dominant search provider a decade from now could easily have revenues of $20 or $30 billion per year.

Google Versus Microsoft

Who will win? Google certainly has impressive assets. Moreover, Microsoft does not own the server side of the Web and probably never will. Nor does it control the architectures of the newer computing platforms, whose markets are growing much faster than the PC's. And in these newer markets, Microsoft faces a painful choice: either provide search technology that will run on, and thereby support, competing platforms such as Linux machines, or let others take the lead.

Yet Microsoft's control of Windows, Internet Explorer, and Office is a real advantage. For instance, if desktop search tools enjoyed deeper access to the internal document structures of Word and Excel, they would be much more useful. Similarly, operating systems can potentially collect information about user behavior that could improve search tools substan-

tially. Other recent search innovations are really enhancements to the Web browser. Google, Ask Jeeves, A9, Blinkx, Yahoo, and Microsoft are all providing search toolbars that can be downloaded into the browser, and independent developers have created many search-related enhancements to the open-source Firefox browser.

But we know who really owns the browser. Ramez Naam, group program manager for MSN Search, declined to say whether or not search functions would be integrated directly into Microsoft's Internet Explorer. But a Microsoft executive, who asked to remain unnamed, told me that his company had recently reconstituted its browser development organization. "Microsoft effectively disbanded the Internet Explorer group after killing Netscape," he said. "But recently, they realized that Firefox was starting to gain share and that browser enhancements would be useful in the search market." He agreed that if Microsoft got "hard-core" about search (as Bill Gates has promised), then, yes, Google would be in for a very rough time.

Why? Because in contrast to Microsoft, Google doesn't yet control standards for *any* of the platforms on which this contest will be waged—not even for its own website. Although Google has released noncommercial APIs—which programmers may use for their own purposes, but not in commercial products—until recently, it avoided the creation of commercial APIs. In late 2004, however, Google announced APIs for its advertising systems and for the Google Deskbar. The advertising APIs could help create an infrastructure of firms dependent on Google's platform and specializing in the management of automated, Web-based advertising strategies. This could protect Google's advertising revenues against future price competition from Microsoft. The Google Deskbar APIs, likewise, should encourage third parties to create search functions for the Windows desktop.

These steps, however, are at best half-measures. Google has not yet faced the need for full architectural competition and in some respects has arguably been moving in the wrong direction. It still has not provided open APIs for its core search engine. (Raúl Valdés-Pérez, Vivísimo's CEO, says that he tried to license Google's search engine services but was refused.) Furthermore, it sells its search software

to enterprises only in the form of a bundled, Linux-based hardware system. This alienates other hardware and software vendors, leaves most of the non-Linux market unserved, and presents a huge opportunity for Microsoft.

Google may feel that APIs are of secondary importance in its coming war with Microsoft. Two Google employees (both of whom prefer not to be named) told me that Google's leaders believe that the company's expertise in infrastructure—knowing how to build and operate those 250,000 servers—constitutes a competitive advantage more important than APIs or standards. This could be a major, even fatal, error. Microsoft can certainly obtain or cultivate the skills necessary to operate large-scale computing infrastructures; indeed, it already operates MSN, with nearly 10 million users.

Worse, Google may feel that APIs can wait. Peter Norvig, the company's director of search quality, told *Technology Review*, "We've had the API project for a few years now. Historically, it's not been that important: it's had one person, sometimes none. But we do think that this will be one important way to create additional search functions. Our mission is to make information available, and to that end we will create a search ecology. We know we need to provide a way for third parties to work with us. You'll see us release APIs as they are needed."

Those words do not convey much sense of urgency. There is, however, another possibility: Google understands that an architecture war is coming, but it wants to delay the battle. One Google executive told me that the company is well aware of the possibility of an all-out platform war with Microsoft. According to this executive, Google would like to avoid such a conflict for as long as possible and is therefore hesitant to provide APIs that would open up its core search engine services, which might be interpreted as an opening salvo. The release of APIs for the Google Deskbar may awaken Microsoft's retaliatory instincts nonetheless. For Google to challenge Microsoft on the desktop before establishing a secure position on the Web or on enterprise servers could be unwise.

Strategies and Prescriptions

In all of Microsoft's successful battles, it has used the same strategies. It undercuts its competitors in pricing, unifies previously separate markets, provides open but proprietary APIs, and bundles new functions into platforms it already dominates. Once it has acquired control over an industry standard, it invades neighboring markets.

In contrast, the losers in these contests have usually made one or more common mistakes. They fail to deliver architectures that cover the entire market, to provide products that work on multiple platforms from multiple companies, to release well-engineered products, or to create barriers against cloning. For example, IBM failed to retain proprietary control over its PC architecture and then, in belatedly attempting to recover it, fatally broke with established industry standards. Apple and Sun restricted their operating systems to their own hardware, alienating other hardware vendors. Netscape declined to create proprietary APIs because it thought Microsoft would never catch up. Google—and Yahoo—would do well to take note.

What will Microsoft do? Publicly, it doesn't care about building a broad search architecture reaching across many platforms. "There will be a lot of innovation and competition around search by a broad number of vendors, but it is wishful thinking to believe it is a platform tidal wave like the initial emergence of the browser and the Web," says Charles Fitzgerald, Microsoft's general manager of platform strategy. And indeed, Microsoft has begun innocently enough: a decent though unspectacular search site, some software, no bundling—nothing, you know, *violent*. But the company will provide APIs to its Web search engine, and its long-term

strategy could be brutal. If it acts logically, it will bundle better search facilities into Internet Explorer and Office; it will build advanced indexing and searching tools into both its PC and server operating systems; and it will alter its own products to make searches of many kinds more fruitful. Search tools could tailor results to a user's interests, based upon data collected by the operating system. Microsoft could even deliberately cause failures in Google's products—for example, altering its file formats so that Google's crawlers could not properly index Word or Excel files. Microsoft has been accused of such conduct repeatedly in the past, notably in its battles against the DR-DOS operating system (an attempted clone of MS-DOS) and Lotus spreadsheet software.

So what should Google do? Given Microsoft's ferocity in the past, panic might be a productive first step.

If it acts logically, Microsoft would also perform a "cashectomy" on Google—just as it did in the browser wars when it gave away Internet Explorer. Even with nearly $2 billion in cash, Google is vulnerable to this tactic. For instance, Microsoft could offer free wholesale access to its search engine. Then it could attack Google's advertising networks by offering free or subsidized advertising placement. These businesses are based primarily upon agreements with third-party websites, most of which have no long-term allegiance to Google. (Google's forthcoming advertising APIs could, however, change this.) Finally, Microsoft will try to play competitors off against each other, as is its custom. Microsoft thrives when its opponents are fragmented and possess no alternative common standard.

So what should Google do? Given Microsoft's ferocity in the past, panic might be a productive first step. Google should understand that it faces an architecture war and act accordingly. Its most urgent task must be to turn its website into a major platform, as some other firms have already done. Amazon, as we have noted, does not merely operate a retail website. It has developed proprietary but open APIs that have made it the capital of an electronic economy *(see "Amazon: Giving Away the Store," p. 28)*. Other merchants set up stores under the Amazon umbrella, and other websites can offer direct links to Amazon's product pages. Recently, Amazon has gone even further, creating ways for consumers to search and find products without visiting Amazon at all.

Thus, Google should first create APIs for Web search services and make sure they become the industry standard. It should do everything it can to achieve that end—including, if necessary, merging with Yahoo. Second, it should spread those standards and APIs, through some combination of technology licensing, alliances, and software products, over all of the major server software platforms, in order to cover the dark Web and the enterprise market. Third, Google should develop services, software, and standards for search functions on platforms that Microsoft does not control, such as the new consumer devices. Fourth, it must use PC software like Google Desktop to its advantage: the program should be a beachhead on the desktop, integrated with Google's broader architecture, APIs, and services. And finally, Google shouldn't compete with Microsoft in browsers, except for developing toolbars based upon public APIs. Remember Netscape.

When Google's Peter Norvig was read this list—presented not as recommendations, but as things that Google *would* do—he did not deny any of it. When *Technology Review* asked, "If we reported any of this, would we be wrong?", Norvig answered, "We don't like the word 'beachhead.' That implies a war, and we don't want to go there." Pressed, he said, "Factually, nothing wrong"—although he stressed that APIs were only one way Google might create a "search ecology." But historically, proprietary APIs have been the only way to create a loyal customer base—one that can't readily switch to a competitor.

Big Questions

Would such an architectural strategy work? I'm not sure, but I think so. I also suspect that if Google doesn't do something like this fast, and Microsoft attacks, Google will go down. Its decline would take longer than Netscape's precipitous descent, but it would be no less final. And at least during the second term of the George W. Bush administration, it is highly unlikely that antitrust policy would come to the rescue.

Whether Google or Microsoft wins, the implications of a single firm's controlling an enormous, unified search industry are troubling. First, this firm would have access to an unparalleled quantity of personal information, which could represent a major erosion of privacy. Already, one can learn a surprising amount about people simply by "googling" them. A decade from now, search providers and users (not to mention those armed with subpoenas) will be able to gather far more personal information than even financial institutions and intelligence agencies can collect today. Second, the emergence of a dominant firm in the search market would aggravate the ongoing concentration of media ownership in a global oligopoly of firms such as Time Warner, Bertelsmann, and Rupert Murdoch's News Corporation.

If the firm dominating the search industry turned out to be Microsoft, the implications might be more disturbing still. The company that supplies a substantial fraction of the world's software would then become the same company that sorts and filters most of the world's news and information, including the news about software, antitrust policy, and intellectual property. Moreover, Microsoft could reach a stage at which its grip on the market remains strong, but its productivity falls prey to complacency and internal politics. Dominant firms sometimes do more damage through incompetence than through predation.

Indeed, as so many have noted, much of Microsoft's software is just plain bad. In contrast, Google's work is often beautiful. One of the best reasons to hope that Google survives is simply that quality improves more reliably when markets are competitive. If Google dominated the search industry, Microsoft would still be a disciplining presence; whereas if Microsoft dominated everything, there would be fewer checks upon its mediocrity. ■

**Disclosure: As the result of selling Vermeer Technologies to Microsoft in 1996, Charles Ferguson still holds a substantial quantity of Microsoft stock, a position which is partially but not completely hedged. He has no other financial interest relevant to this article.*

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The Problematical Dr. Huang Hongyun

Can an experimental technique using fetal-cell transplants help paralyzed patients? Probably not.

BY HORACE FREELAND JUDSON

ANESTHETIZE THE RAT. Lay it belly down. Shave a patch along its spine and cut to the bone. Do a laminectomy, that is, take the bone off a short length of the back of the spine, exposing the spinal cord. Suspend a 10-gram rod above the spinal cord, at a height of 12.5 millimeters, or 25, or 50 millimeters. Let it drop.

The result will be a bruise, or more technically, a contusion, of the rat's spinal cord. The bruise interrupts nerve transmission, paralyzing some muscles and blocking sensation. The location and severity of the damage will depend on the site of the blow and the height of the drop—and the consequent behavioral changes are reproducible. The procedure was developed in the early 1990s in the laboratory of Wise Young, a neurologist then working at New York University and now at Rutgers. He wanted to create a model for spinal-cord injury, in order to test and evaluate proposed treatments to repair the damage and restore some degree of function. Not long before, three scientists at Ohio State University had devised a rating scale for precise scoring of loss of function in spinal-cord injury. Young adapted the scale to his rat model, based on how well or poorly an injured creature could walk. In 1995, he showed that the behavioral rating varies in direct proportion with tissue damage at the injury site. In a recent conversation, he said, "This was the first behavioral outcome measure that correlated with morphological damage in the spinal cord." Although no one measure is universally accepted in spinal-cord-injury work, Young said, "This comes close."

The spinal cord is remarkably well protected, by bone and by its tough outer layer, the dura. In humans, only about 10 percent of spinal-cord injuries, caused by mishaps like a bullet through the spine, interrupt the cord completely. Ninety percent are contusions. Nerves in the adult central nervous system, including the spinal cord, do not spontaneously regenerate. Some nerves in the peripheral system,

ILLUSTRATION BY STANLEY MARTUCCI

however, can—importantly, in the presence of Schwann cells, a type of cell that provides an environment favorable to new growth of nerve axons. Many attempts have been made to transplant such cells into damaged spinal cords, to promote regeneration, but they have all failed.

Enter *olfactory ensheathing glial cells*—bearing the hope of a way to fix, or at least to ameliorate, spinal-cord injuries. In 1984, Ron Doucette, at the University of Saskatchewan, described a new kind of cell, which he had found in the olfactory nerve and the olfactory bulb. The olfactory nerve is the only central-nervous-system nerve that continually regenerates throughout adult life. It is made up of neurons that arise in the mucous tissue of the nose and run the short distance to the olfactory bulb, one of the most primitive parts of the brain.

We sniff substances all the time that are toxic to these neurons, which die and must be replaced. New ones are constantly being generated. They send axons up the olfactory nerve to establish fresh connections to the bulb. Doucette's new-found cell produces a particular protein that marks it as a glial cell—a class of support cells, which include Schwann cells, that surround neurons. The surface of Doucette's cell carries what are called cell-adhesion molecules, which attract growing axons. In the years after his discovery, Doucette isolated these cells and learned to grow them in tissue culture. He found that they wrap around axons and promote their growth: hence the name, olfactory ensheathing glial cells. In 1990, Doucette proposed that they are the principal reason the olfactory nerve can regenerate. Then and today, he has been pursuing how exactly Schwann cells and ensheathing cells do what they do.

The exciting question was whether the glial cells might encourage regrowth of spinal-cord neurons. Several scientists jumped on it, conspicuously Almudena Ramón-Cueto of the Universidad Autónoma de Madrid in Spain and Geoffrey Raisman at the National Institute of Medical Research in London.

Ramón-Cueto first tried cutting the peripheral nerves of rats at the point, called the spinal root, where they connect with the spinal cord. Such injuries are crippling. Normally the nerves will not grow back into the spinal cord. She then transplanted some of the creatures' own olfactory ensheathing glial cells into the region of the root, and in 1994, she claimed that this allowed the nerves to regenerate their connections. She then went to work with Mary Bunge of the Miami Project to Cure Paralysis, which is at the University of Miami. Bunge's main approach has been to graft Schwann cells into rats' spinal cords, bridging spinal lesions, and then to try various measures, including drugs in different combinations, to get them to grow. In 1998, she and Ramón-Cueto injected adult-rat olfactory ensheathing glial cells into the areas at each end of the Schwann bridges. They reported that six weeks after the combined graftings, spinal-cord axons were growing through the Schwann cell bridges and beyond—and that the ensheathing cells had migrated, accompanying growing axons through and alongside the Schwann bridges.

Raisman, meanwhile, was also experimenting with olfactory ensheathing glial cells. In 1985, he had suggested that these cells had special properties that enabled them to repair central-nervous-system neurons. Now, in a clever experiment, he used a thin electrode to burn through rat spinal cords on one side only, at a point that left the creatures able to use only one forepaw. Before the operation, he had trained the rats to reach through a hole for pellets of food with their forepaws, using one or the other with equal facility; afterwards, they were unable to reach with the affected limb but could use the other normally. He then transplanted into the spinal lesions a mixture of cell types, including olfactory ensheathing glial cells. In 1997, Raisman and colleagues reported in *Science* that as early as ten days after the transplants, spinal-cord axons sprouted and grew across the lesions. Two to three months after the transplants, of a group of seven rats, four were able to use either forepaw as adeptly as normal rats. Dissection showed that these four had regrown spinal-cord axons across the lesions.

In 2000, after returning to Spain, Ramón-Cueto published a paper in the journal *Neuron* asserting that when she transected the spinal cords of rats and injected olfactory ensheathing glial cells into the lesions, many of the rats recovered some locomotor function. The degree of regeneration and recovery was slight, and some raised questions about exactly how she did the tests. Yet the paper had impact.

The pressure is now intense to get to clinical trials. The United States alone has on the order of 200,000 patients with spinal-cord injuries. (Their plight was dramatized by Christopher Reeve, the quadriplegic Superman and spinal-cord campaigner, who died on October 10, 2004.) Raisman is pushing toward trials, as is Ramón-Cueto. In June 2003, Raisman told the BBC, "My guess is we are probably two to three years away. It could be less." A group in Brisbane, Australia, led by Alan Mackay-Sim, has duplicated the rat experiments with ensheathing cells and is at the stage of exploratory clinical trials; Carlos Lima, from the Egaz Moniz Hospital in Lisbon, has treated a small number of patients. Yet extreme caution is obviously necessary: the procedure raises great scientific, medical, regulatory, and ethical problems. In a recent telephone conversation, Doucette emphasized repeatedly that the basic physiology is still not understood. "Just putting the cells in and saying, 'Oh, great, we've got some functional recovery,' and then moving on to the next step, to me isn't satisfactory. I want to know how it happened. Why. And how you can control it," he said. He went on: "My view is that I think we're probably five, ten years away. In terms of being at a stage where I'm confident we know enough about what's going on."

Enter Dr. Huang Hongyun.

The Paper

In 1999, a Chinese neurosurgeon named Huang Hongyun arrived at New York University School of Medicine from Beijing, wanting to work with Wise Young and learn about spinal-cord injury. Young had moved to Rutgers, so Huang followed him there. "He wanted to know what to do," Young said. "Studies recently published had claimed that olfactory ensheathing glial cells transplanted into spinal cords would regenerate rats and improve locomotor recovery. I was skeptical about some of the results. They were mostly based on, I thought, fairly questionable behavioral outcome measures. So I suggested to him, Why don't we do it in our spinal-cord injury model?" Huang worked with Young for several years, then moved back to Beijing, becoming chair of neurosurgery at Chaoyang Hospital.

Almost at once, Huang began operating on human patients with injured spinal cords. In March 2003, he and colleagues

submitted a four-page paper to the *Chinese Medical Journal*, which published it in October of the same year.

The journal is something of a historical oddity. It comes out monthly, about 100 pages an issue, entirely in English except for contributors' names. It was founded in 1887 by missionaries who wanted to bring Western medical methods and standards to China and needed an English-language publication that would present the best of modern Chinese medical research and clinical practice. In the first half of the 20th century, it was well respected; after the Communist takeover of mainland China, it declined badly. Only in the last five years or so has the journal begun to regain quality and the respect of non-Chinese scientists. But scientists do not consider the journal to be peer reviewed—at least, not to Western standards. Submitted manuscripts may be looked over by various senior medical-faculty members, but if anything, this is a liability, for a uniquely Chinese reason: Confucian tradition still inculcates profound respect for elders. To turn down a paper submitted by a senior person would be an act of disrespect.

Huang's paper reported results of surgery on 171 patients, 139 male and 32 female, ranging in age from 2 to 64 years, with the average age just under 35. All had suffered extensive paralysis and loss of sensation. The time since injury was at least six months and as much as 18 years. All had received previous therapy of one sort or another, for example, administration of nerve-growth factors and surgery, if that had been necessary to relieve pressure on the spinal cord. A requirement was that magnetic-resonance imaging showed no gap in the spinal cord and no compression.

The surgical procedure*, which the paper described in detail, is essentially to perform a laminectomy at the site of the damage, open the dura, and inject ensheathing cells. These Huang derived from olfactory bulbs. Although the paper does not mention this, in later discussions Huang has said that the cells come from fetuses aborted in the fourth month of pregnancy. (But they are not stem cells, as has sometimes been reported.) He grows them for two weeks in cell culture, as he learned to do in Young's lab. He then injects 50 microliters of a cell suspension, approximately half a million cells, into the spinal cord, next to the ends of the lesion.

Before the operation, patients were assessed for degree of paralysis and for sensitivity to light touch and to pinpricks, following an international standard. They were reassessed between two and eight weeks later. The paper claimed that patients made significant if relatively slight improvement in these measures. However, the data are scanty and impossible to evaluate reliably. The subjects are grouped by age but not differentiated further, not even, say, into male and female. The paper describes no individual cases. It offers no before and after scores, just degrees of improvement, and these as averages within each age group. It says nothing about possible deleterious effects, not even that there were none. It reports no long-term outcomes.

Huang's paper says nothing about possible deleterious effects, not even that there were none. It reports no long-term outcomes.

Huang has published nothing more.

Sound and Fury

The report drew immediate and intense attention. Discussion groups sprang up on the Internet; within weeks, thousands of patients from the United States and elsewhere had got in touch with Huang. First to report the story in print was Jerome Groopman, at the *New Yorker*, in a profile of Christopher Reeve published on November 10, 2003; he described a range of animal experiments that Reeve was following, including Young's and especially Ramón-Cueto's, and gave five paragraphs to the promise of Huang's work and some of its problems.

In February 2004, in Vancouver, British Columbia, a consortium called the International Campaign for Cures of Spinal Cord Injury Paralysis held a two-day international workshop on clinical trials. Several speakers presented preliminary results of treatments involving drugs. Three spoke of clinical trials involving olfactory ensheathing glial cells, surgically implanted. Mackay-Sim, from Brisbane, described an initial human trial testing the safety of his procedure. He used ensheathing cells from each patient's own mucosa, purified and grown for six weeks in culture, then injected at 40 small sites in and around the patient's spinal lesions. Four patients got transplants; four got placebos. His assessments before and afterwards were elaborate and blind, the best in the business so far. Results were not yet in. Lima, from Lisbon, reported that he had treated seven patients by taking portions of their own olfactory mucosae, containing many sorts of cells, and transplanting these directly into spinal-cord lesions. Improvements were minimal, and one patient got worse. Lima used no placebos, and assessments were not blinded.

Huang reported his work—announcing that he had now given fetal-olfactory-ensheathing-cell transplants to more than 300 patients, including a number of Americans and other Westerners. Some patients, Huang said, showed improvements two or three days after the operation, although all experimental evidence said that nerves could not regrow that fast. He had tried no placebos; his assessments were unblinded and were thought rudimentary. He reported no adverse consequences, although with so many cases that was implausible. Follow-up was minimal and never conducted more than a few months after the procedure. The ethical risks were obvious and considerable.

James Guest and Eva Widerstrom-Noga, both physicians working with the Miami Project to Cure Paralysis, attended the Vancouver meeting. They came home with grave reservations; nonetheless, Bunge and her colleagues decided they needed to know more. They invited Huang to come to Miami.

Media attention built. On April 13, the Detroit *Free Press* ran a story about the Rehabilitation Institute of Michigan, located on the campus of the Detroit Medical Center. The previous fall, the institute had announced it would screen patients for possible operations in China or Portugal.

* **WWW.TECHNOLOGYREVIEW.COM** We put together an illustrated guide to how Huang Hongyun's procedure works. Keyword **fetal cell.**

After that, two patients had gone abroad, Robert Smith to Beijing and Erica Nader to Lisbon. While in the United States, Huang had visited the Rehabilitation Institute. Now with a waiting list approaching a hundred, the institute said that in August it would open an outpatient center where applicants would be evaluated and patients returning from China or Portugal would be monitored. The institute was already following up with Smith and Nader, and the newspaper's account of their progress, though cushioned with language like "steady progress" and "long road to recovery," was glowing.

That same day, public broadcasting stations aired an hour-long program called "Miracle Cell," part of the starry-eyed series *Innovation*. Though it didn't mention Huang, the program presented Lima's work in Lisbon, enthusiastically overstating the progress his patients had made, and gave Raisman in London a platform from which to announce his plans for clinical trials. "Miracle Cell" repeatedly confused fetal olfactory ensheathing glial cells with stem cells.

Huang lectured at the Miami Project on May 5, 2004. Guest arranged to visit him for 10 days in July, accompanied by Tie Qian, a physician specializing in physical medicine and rehabilitation with the Miami Veterans Affairs Medical Center who is Chinese and speaks the language.

The second week in June, Tim Johnson, a reporter for the Knight Ridder News Service, filed an article from Beijing about Huang, his hospital, and his claims. It was picked up by a number of papers in the chain, including the Lexington, KY, *Herald-Leader* and the Miami *Herald*. On July 30, the *Scientist*, a weekly magazine of science news and features, carried an article about Huang. The Asian edition of *Time* ran a similar story from Beijing in its August 16 issue.

On August 27, the Chicago *Tribune* ran an article by Michael Lev that began, "A Chinese neurosurgeon has been besieged by desperate Americans willing to pay $25,000 for an implant of cells from aborted fetuses, a controversial and scientifically unproven procedure." The piece was more thorough than most in voicing the uncertainties and reservations about Huang's claims. Yet febrile publicity and desperate hope were by that time driving the public response. In Lev's article Huang claimed that he had performed 450 transplants, while the waiting list for his procedure had grown to more than a thousand, including a hundred Americans.

A House Call

At half past eight on the morning of Friday, September 10, 2004, a meeting began at the laboratories of Massachusetts General Hospital. Huang was to speak. The meeting was limited to physicians and scientists. The chief organizer was Robert H. Brown, a professor of neurology at Harvard Medical School and director of the Day Laboratory of Neuromuscular Research at Mass. General. I had spoken with him by telephone early in the week; he told me he was skeptical.

Huang is of medium height, with a receding chin, and seemed somewhat diffident. His English is limited and strongly accented. He was there, it turned out, not to present his work on spinal-cord injury but to discuss another project that, he said, he had begun 18 months earlier. The title of his talk was "Olfactory Ensheathing Cell Transplantation for Amyotrophic Lateral Sclerosis." ALS is the devastating nerve disorder better known as Lou Gehrig's disease. (The accounts in the *Scientist*, *Time Asia*, and the Chicago *Tribune* had mentioned Huang's turn to ALS.) Huang offered some minimal PowerPoint slides. His summary claim, at beginning and end: "OEC transplantation is safe, feasible, and rapidly improves partial function. Results are observable in two or three days, and improvement continues for two to three months. The mechanism is unclear." However, his data were shockingly thin—indeed, insultingly so, I came to think. He finished up with half a dozen brief, blurry before-and-after videos of six of what he said had been a set of eight ALS patients, newly able to walk, or to stand, or to sit up, or to move the tongue enough to talk, if indistinctly. Each was followed by charts depicting nerve function before and after the transplant surgery.

His audience treated him with caution and courtesy, while its skepticism and impatience steadily increased. Much of the simplest factual information—predata, one might call it—was missing. Halfway through the question period, I asked several questions. When did his work with ALS patients begin? January 2003, he answered. But the videos carried dates, and these were as recent as mid-August 2004, just three weeks earlier. How many patients had he treated? He gave no clear answer; after follow-up questions from others, the likely number seemed to be 10 or 11—until he said there had been "about 40." Did they all get fetal cells? No answer.

As the questioning went on, problems with Huang's methodology seemed to emerge, chiefly the lack of rigorous pre- and postoperative evaluation of patients' functioning, the lack of controls, and, above all, the total absence of follow-up beyond a few months.

On his home ground, Huang is more assured, smoother. Indeed, with Chinese patients, he evinces a certain quiet charisma.

On his home ground, Huang is more assured, smoother. Indeed, with Chinese visitors and with patients, he evinces a certain quiet charisma. Chaoyang Hospital, Beijing, is part of a set of gray, grimy stone buildings around a gated courtyard, with no clear indication of which is its main entrance. Huang's office is on the hospital's top floor, but we met on the second, in a serviceable workroom with a central set of tables and, around the walls, shelves haphazardly filled with equipment and supplies. The room sits at the head of a dim corridor along which open, on either side, wards with six beds each, some empty, some occupied by patients, though not all are spinal-cord cases. The patients are surrounded by members of their families—as is customary in China, where much of patients' care falls to relatives.

Huang and I discussed his procedures in detail. Some who had heard him in the United States wondered whether the cells he implanted were a raw mixture or purified. "We get the olfactory bulb out," Huang said. "Of course, mixture. Then we culture them and purify them." The dose for a spinal-cord patient is one million cells, "90 percent OEG cells." Had he published anything about safety? He

ducked the question at first, then said that the cells caused "no long-term fever." He elaborated: "No problems with the cells; maybe we have complications of the surgery—infection of the area, leakage of the cerebrospinal fluid. The general complications of other surgery."

How much did patients gain? Again, he ducked. Before and after the procedure, he said, patients were evaluated by three doctors, according to standard protocols, for movement, for control of the anal sphincter, and for sensitivity to touch and pinprick. Did any patients have adverse reactions? "Ah, a very complicated question." But then, "In actual score, no patient got worse." But the degree of improvement? These patients are in bad shape, he said. "Any improvement is a bonus." Any complete cures? "I don't think it is possible to cure this disease." Even when progress is minimal and gradual, Huang said, it is valuable. "Complete chronic injury, no chance to get 100 percent."

Critics in the United States have suggested that any patient with spinal-cord injury or, for that matter, ALS who comes to a medical center for some major procedure will probably get a variety of other treatments at the time, and this by itself might provoke temporary improvement. Did patients at Chaoyang Hospital get other treatment as well—such as physical therapy or other rehabilitative help? "No," Huang said. Physical therapy is not routine in China. "They go home."

What about follow-up? "They start to improve in two or three days. Then we follow them in two to four weeks. Then another follow-up three to six months." But what about the longer term? Again, critics have held that patients ought to be tracked for at least two years. Huang hesitated. Then, "Chinese patients very poor. They go home." He said he could not get in touch with them again.

Had Huang tried to publish other papers, and in peer-reviewed Western journals? Several, he said, but so far no response. He was collaborating on a paper with Guest and Qian from the Miami Project. During their visit to China, Huang said, "They evaluated one patient" before and after surgery. "Totally paralyzed. After surgery, can do this, can do this"—he was making small finger and hand motions. How quick was the recovery? "Second day after, Dr. Guest and Dr. Qian saw some difference." What could possibly be the mechanism for change that soon? "In front of all eyes, we saw some change, even though they know we couldn't explain it." In mid-October, Guest sent the completed case report to Huang, but a month later Huang still had not found time to look at it.

Huang told me that hospital policy prohibited my watching the surgery. Guest and Qian during their visit examined 12 spinal-injury patients. They formally assessed six of them before and after and indeed observed four operations. They acknowledge that some of the patients demonstrated a degree of modest improvement in motor and sensory function—and that the improvement occurred surprisingly soon. However, two patients showed "wound breakdown," one of them suffering "a reduction in leg function." A third patient came down with meningitis. "The Chinese clinicians did not record these complications in the medical record," asserts an unpublished report by the Miami Project. Although Guest and Qian did watch surgery and observe patients, they were not allowed into the laboratory where the cells for transplantation were prepared and had no way to know the content of the putative human fetal olfactory-bulb cultures—not even whether the material transplanted actually contained ensheathing cells. Guest adds, "We did see one set of cultures that showed robust cell growth and morphology that could be ensheathing glia. They were very healthy cultures. We viewed them in Dr. Huang's clinical office." The chief problem they saw, however, was the lack of long-term follow-up, including full records of any adverse effects.

To me, the most disturbing sign was Huang's evasiveness. He pleaded repeatedly that patients needed to be treated: "These are suffering, dying people. I am a surgeon. The first thing is to save lives and alleviate suffering." Though this sentiment may be genuine in Huang's case, such evasions are a classic mark of the charlatan. Alternatively, he asserted that important types of controls (for example, surgery that mimicked the operation but injected not cells but salt water) would be dangerous and unethical. He insisted repeatedly that the procedure is safe.

Huang's methodology is a moving target: from work with spinal-cord lesions to ALS, from injections into the spinal cord to injections into brain tissue. Critics have demanded that the procedure involve a fixed quantity of injected cells, one or a few standard points of injection, and significant blinded controls, and that evaluation follow a standardized protocol, including, for example, rigorous pre- and postoperative physiological tests that measure such properties as breathing, muscle tone, and strength.

Deadly Decisions

Despite the defects in Huang's work, no definitive judgment is yet possible. Wise Young is a cautious advocate. He notes, "There are really no randomized clinical trials for any of the current neurosurgical procedures." Regarding Huang's work, "The big debate right now is, What is the level of evidence that's necessary and sufficient to take something to clinical trial?" Meanwhile, though, when dealing with spinal-cord patients and their families, "My official recommendation is that they should wait. Many of them ignore me; they go on ahead to do it anyway." Mary Bunge and her colleagues at the Miami Project find Huang's claims frustrating. "Presently, Dr. Huang's project by research standards in the United States is not a clinical trial but is a clinical treatment series. The treatment series does not meet the design standards for a clinical trial that would allow for definitive results to be obtained." Yet they call for "independent and impartial assessment of the risks and benefits of this cell therapy." Meanwhile, though, "Miami Project faculty do not endorse this procedure and at this time would not advise individuals to undergo this surgical transplantation strategy. While some people with SCI will view these current experimental procedures abroad as their only hope, by participating they may be putting themselves in harm's way."

The science of Dr. Huang Hongyun raises to our awareness this deep tension over standards of evidence and the ethics of clinical practice.

I saw Huang the afternoon of October 20, 2004. A correspondent from the Mobile, AL, *Register*, Karen Tolkkinen, was also in Beijing, Huang said; he was to treat several Americans with ALS that week, and one was from Alabama. That evening, he operated on Ronnie Abdinoor, a 47-year-old from New Hampshire. On October 29, Tolkkinen reported in the *Register* that Abdinoor had died. ■

What We Can Learn from Robots

For Japan's Mitsuo Kawato, robotics explains how the human brain works.

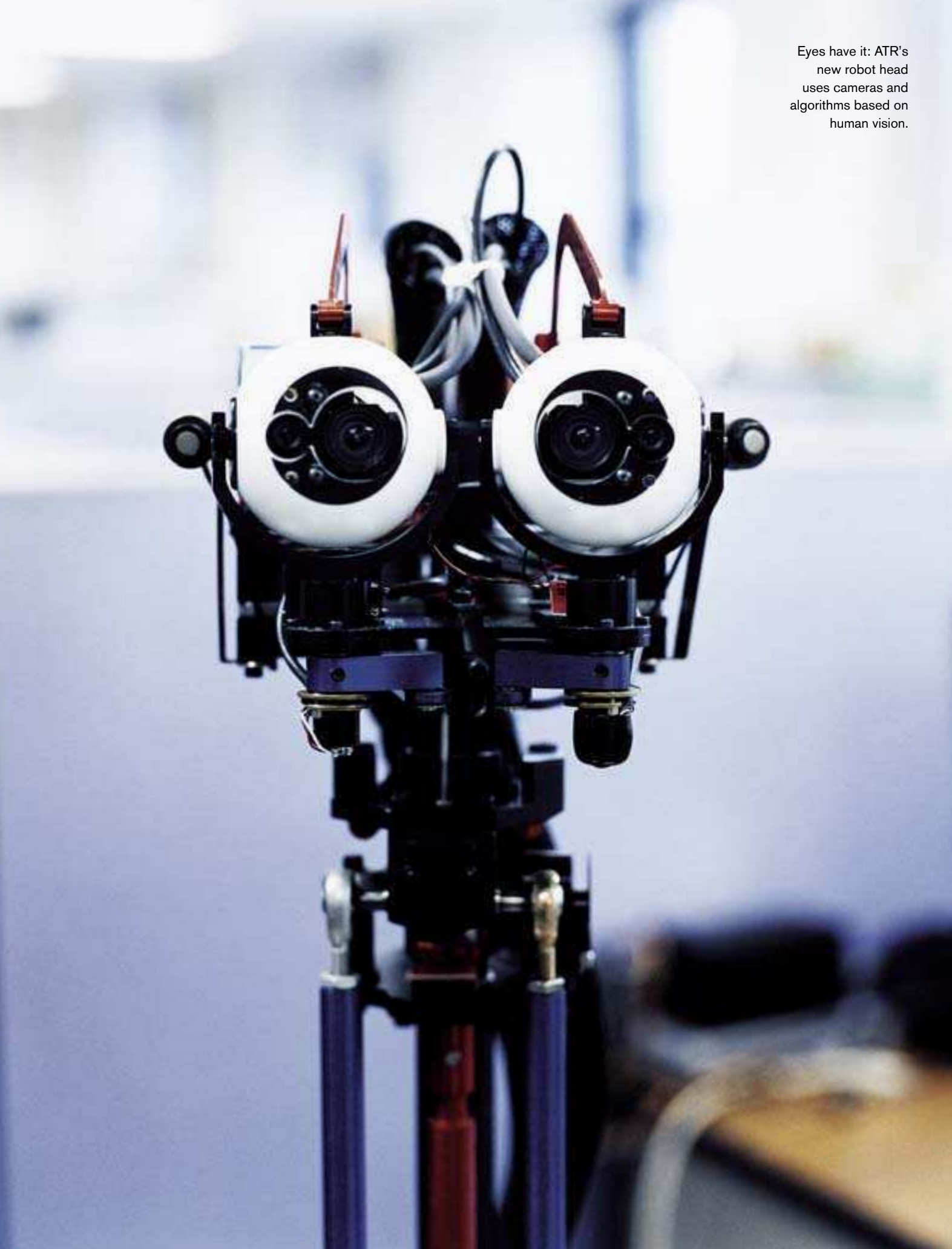
BY GREGORY T. HUANG

PHOTOGRAPHS BY GRAHAM MACINDOE

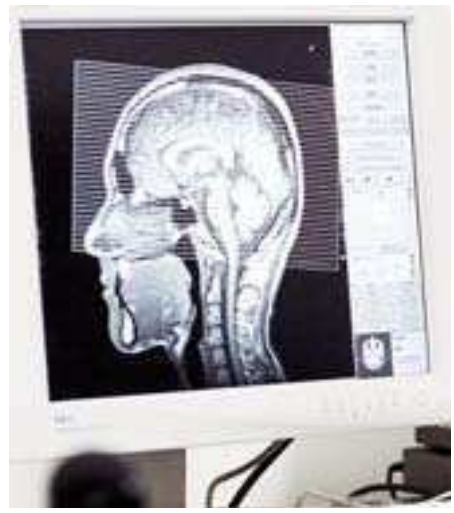
ON A CRISP OCTOBER DAY LAST YEAR, Carnegie Mellon University's Robotics Institute kicked off its 25th-anniversary celebration, as the world's robotics experts came to Pittsburgh to see C-3PO, Shakey the robot, Honda's Asimo, and Astro Boy inducted into the Robot Hall of Fame. The next day saw demonstrations of running, snaking, and bagpipe-playing bots. On the third day, it was Mitsuo Kawato's turn to speak. The lights went down, and the director of the ATR Computational Neuroscience Laboratories in Kyoto, Japan, made his way to the stage to the beat of rock music.

Despite such a welcome, Kawato is an outsider here, dismissive of the self-congratulation that creeps into conversations about modern robotics. He begins his presentation by shuffling slowly across the stage, imitating how stiffly and deliberately today's humanoid robots walk. What this suggests, he says, is that scientists don't really understand how the human brain controls the body. If they did, they could re-create the process in a robot. Indeed, Kawato doesn't talk about improving robot vision or navigational controls, as many other speakers at the gala do. Instead, he describes the role of brain regions such as the cerebellum and basal ganglia in the acquisition of motor skills, carefully couching his explanations in terms that roboticists understand.

On Kawato's lapel is a button that reads "I ♥ Robots!" But there is a difference between him and other attendees. Kawato loves robots not because they are cool, but because he believes they can teach him how the human brain works. "Only



Eyes have it: ATR's new robot head uses cameras and algorithms based on human vision.


Of machines and men: Using magnetic resonance imaging (left), researchers gain a better understanding of the brain (center), which helps them design better robots (right).

when we try to reproduce brain functions in artificial machines can we understand the information processing of the brain," he says. It's what he calls "understanding the brain by creating the brain." By programming a robot to reach out and grasp an object, for instance, Kawato hopes to learn the patterns in which electrical signals flow among neurons in the brain to control a human arm.

It's a surprising and controversial idea. Despite the increasing number of humanlike machines, robots and people are nothing alike. The human brain has billions of neurons interconnected in complex ways that no computer program can yet simulate. But Kawato believes that experiments on humanoid robots can, at least, provide simplified models of what certain groups of neurons in the brain are doing. Then, using advanced imaging techniques, he looks at whether brain cells in monkeys and humans accord with the models.

"This is very different from the usual justification for building humanoid robots—that they are economically useful or will help take care of the elderly," says Christopher Atkeson, a robotics expert at Carnegie Mellon. Rather, Kawato's motivation lies in using robots to gain insights into how people think, make decisions, and interact with the world. That information could help doctors design therapies for patients with brain injuries, strokes, and neurological disorders—even cognitive and behavior problems. Seeing what it takes to design a socially interactive robot, for example, might motivate a search for areas in the brain that are switched off in cases of autism. (Neural circuits in the basal ganglia are prime candidates.) A robot arm that becomes unstable when feedback signals are delayed might suggest a new source of tremors in the cerebella of Parkinson's patients.

As a tool for understanding the mind, robots are "extremely valuable," says Antonio Damasio, head of neurology at the University of Iowa and the author of three books on the brain that have popularized the notion of "embodied intelligence." "Robots can implement and test how processes like movement can occur," he says. By extending these models to develop a broader theory of the mind, Damasio adds, "we'll know more and more about what it takes for, say, human consciousness to operate."

A robot arm that becomes unstable when feedback signals are delayed might suggest a new source of tremors in the brains of Parkinson's patients.

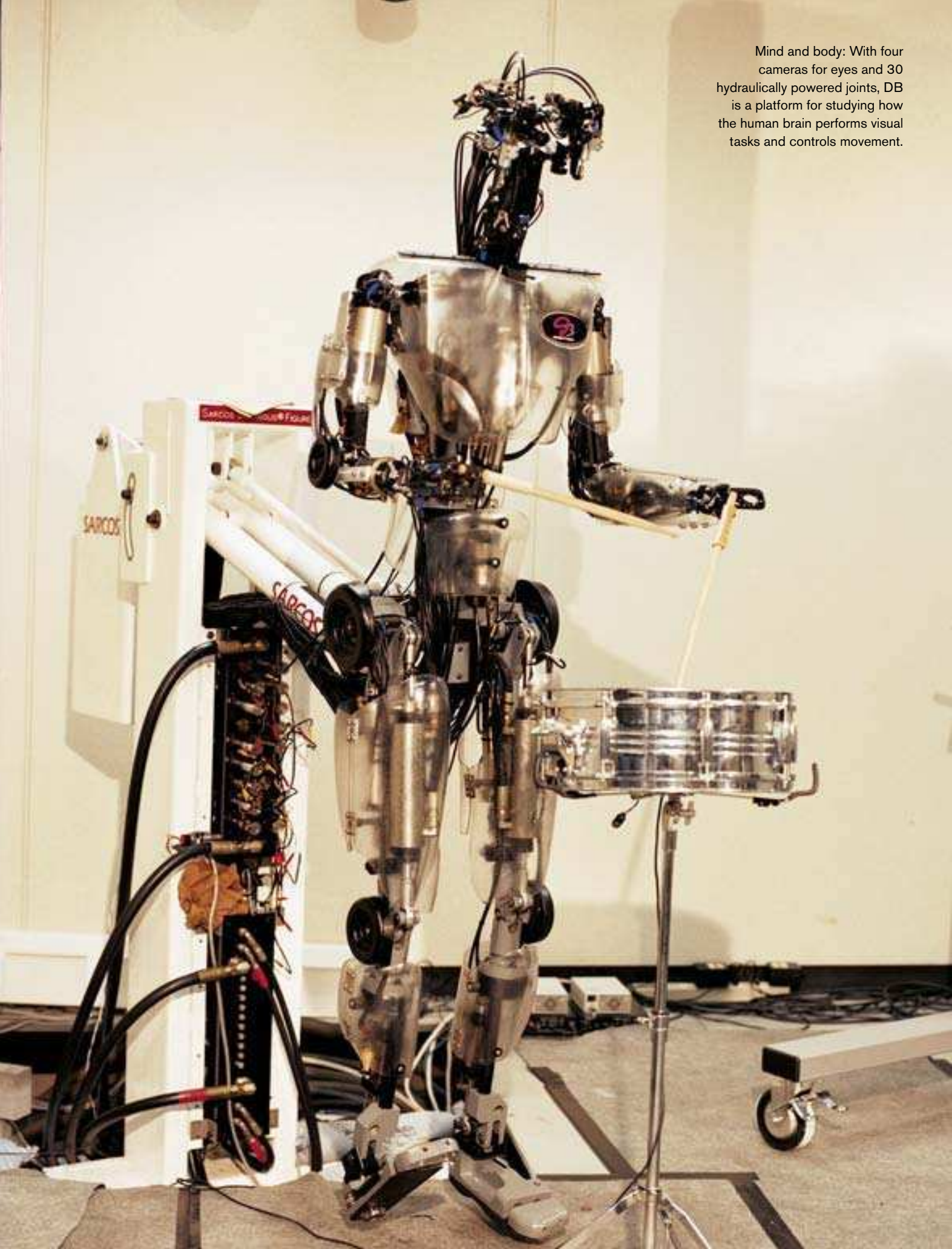
Lost in Translation

There's a Japanese proverb that says, "To teach is to learn." Down the hall from Kawato's office at ATR, robot school is in session. In one corner, a researcher teaches the humanoid robot DB, short for Dynamic Brain, to interact with people. Built like a good-sized person, 1.9 meters tall and 80 kilograms, DB also moves like one: it's fast and graceful. The researcher stands in front of the robot, waving around a stuffed dog. DB watches, apparently intently, tilting its head and tracking the toy with its camera eyes. Then it reaches out with a hydraulic arm and pats the dog, a bit clumsily, on the head. A big screen nearby displays what the robot sees, as well as which algorithms it's running.

But this isn't just another robot showing off its humanlike skills. Gordon Cheng, head of the humanoid robotics group at ATR, thinks of DB as an experimental subject that eats electricity and bleeds hydraulic fluid. Working with robots, says Cheng, teaches "how the pieces fit together to build a rich system" that can emulate the human brain and body.

To control DB's arm, for instance, software computes what commands will produce the right sequence of joint movements to achieve a certain goal. Kawato and Cheng believe a similar process happens in the human brain: they think we use "internal models" to calculate relationships between neural signals and the resulting body movements. For example, when you're about to pick up a cup, neurons in your brain access internal models to figure out what series of signals to send to your shoulder, elbow, and wrist. It's as if your brain were carrying out calculations every time you drink your coffee.

It is a system design that might seem intuitive to a roboticist, but for years most neuroscientists found it ridiculous. How, they asked, could neurons perform such complex computations? They believed the command signals from the brain were much simpler, and that muscles and reflexes—not some abstract model—largely explained motor behaviors. But over the last decade, Kawato has offered strong evidence to the contrary, arguing that internal models are in fact necessary for eye and arm movements and may even



Mind and body: With four cameras for eyes and 30 hydraulically powered joints, DB is a platform for studying how the human brain performs visual tasks and controls movement.

Evolution of Robot Intelligence

While robots have become smarter and more humanlike over the years, robot intelligence remains an oxymoron: robots' utility lags far behind that of their counterparts in the movies.

1921

In the Czech play ***R.U.R.***, humanoid robot workers revolt and destroy humanity.

1951

Japanese cartoonist Osamu Tezuka introduces ***Tetsuwan Atom*** (Astro Boy), a robot who will inspire generations with his superhuman abilities and human emotions.

1961

Unimate, the first industrial robot, joins a General Motors assembly line.

1966

The Stanford Research Institute's ***Shakey***, the first mobile robot with reasoning ability, moves around obstacles using primitive visual processing and artificial intelligence.

1970-1973

Waseda University's ***WABOT-1***, the first humanoid robot, moves its arms and legs and demonstrates basic vision and hearing systems.

1977

Star Wars droids ***R2-D2*** and ***C-3PO*** travel around the galaxy, bicker like an old couple, and help destroy the Death Star.

ca. 1986

Carnegie Mellon's Leg Lab builds ***legged robots*** that balance, run, and do gymnastics-inspired flips, all with relatively little brainpower.

1993

MIT's Artificial Intelligence Laboratory starts building ***Cog***, a humanoid robot that can interact with people and the environment.

1996

Honda unveils its ***P2*** walking humanoid robot, the product of 10 years of secret research (and the precursor to ***Asimo***).

1999

Sarcos and ATR's humanoid robot ***DB*** learns to juggle and imitate human movements.

2003

Sony presents the ***QRIO*** entertainment bot, which can walk, dance, recognize voices, and speak.

2004

IRobot sells its millionth ***Roomba*** robotic vacuum cleaner.

be important for interactions with people and with objects in the world.

In practice, however, it's difficult to draw direct connections between robots and humans. To do so would require the robots and their algorithms to mirror human physiology and neurology as closely as possible. Yet DB's brain doesn't even reside in its head, occupying several racks of computers, and a different scientist is needed to fire up each of the robot's many behaviors, such as reaching or juggling. How DB carries out a task may or may not have much to do with how a human brain operates. To find out, Kawato's team is studying how people learn to solve problems.

In experiments conducted in Kawato's lab, subjects lie in a magnetic-resonance imaging machine and learn to use an unfamiliar tool, a modified computer mouse, to follow a moving target on a screen. Certain areas in the cerebellum light up, indicating increased blood flow in certain clusters of neurons. The researchers believe these neurons represent an internal model of the coördinated actions required for using the tool—much like the ones programmed into DB.

By combining magnetic-resonance imaging, which offers millimeter-level resolution, with electrical and magnetic recording techniques, which resolve brain activity down to milliseconds, Kawato's group hopes to understand more of the details of what is happening among these neurons. It's what Kawato calls "mind decoding"—reading out a person's intent based solely on neural signal patterns. If successful, it would be a breakthrough in understanding how the mind works.

Translating the brain's messages into language that a robot can understand is a step toward realizing a long-term technological ambition: a remote "brain-machine interface" that lets a user participate in events occurring thousands of kilometers away. A helmet could monitor a person's brain activity and report it, over the Internet, to a remote humanoid robot; in nearly real time, the person's actions could be replicated by a digital double. To build the system, researchers will need to look in the brain for specific signals, translate them, transmit the data wirelessly without large delays, and use them to control a device on the other end. The puzzle is far from complete, but Kawato's mix of neuroscience and robotics could at least snap the first few pieces into place.

Robots 'R' Us

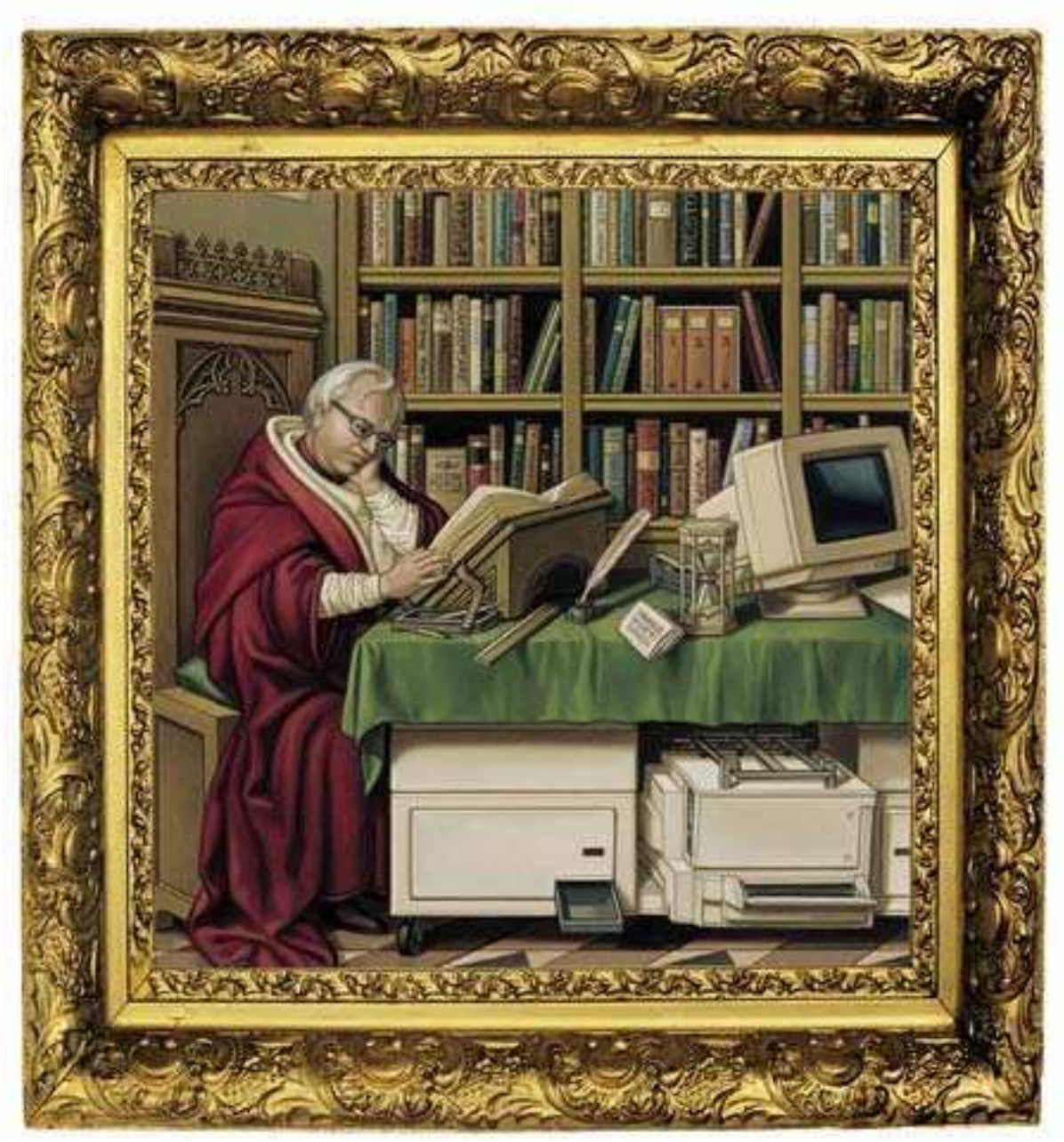
Using robots to understand the human brain could also produce more autonomous robots. That may not be saying much. MIT artificial-intelligence pioneer Marvin Minsky says, "Robots today seem uniformly stupid, unable to solve even simple, commonsense problems." The most successful product from iRobot in Burlington, MA, a leading robotics company, is a vacuum cleaner. Industrial robots paint cars and build microchips but can't do anything they're not programmed to do. But there is increasing interest, especially in Japan and Europe, in developing new humanoid robots using insights from neuroscience.

That development has already begun in Kawato's lab. As part of a five-year, $8 million project, DB is getting an overhaul,* based in part on what Kawato has learned from probing the human brain. The new robot—designed, like DB, by Sarcos of Salt Lake City, UT—will be more humanlike in its anatomy, brain architecture, power requirements, and strength. It will have powerful legs that will allow it to walk and run. (By contrast, the current DB can't walk.) Once the new bot is operational in late 2005, one of its first uses will be as a test platform for studying gait disorders and falls among elderly people.

Kawato is also laying the foundation for a grander collaboration between robotics and neuroscience. Together with Sony and Honda, he is lobbying the Japanese government to help fund a worldwide project to build a humanoid robot that would have the intelligence and capabilities of a five-year-old child. In addition to the technological payoff, says Kawato, the benefits to neuroscience would be immense, though he believes it will take upwards of $500 million a year for 30 years to make it happen.

The evolution of robots into something more humanlike is probably inevitable. Experts agree there is nothing magical about how the brain works, nothing that is too inherently complex to figure out and copy. As Kawato is learning in his lab, the ultimate value in closing the gap between humans and machines might lie in what new generations of robots can teach us about ourselves. ■

* **WWW.TECHNOLOGYREVIEW.COM** To see the brain and body of "DB2" under construction, visit our website and enter keyword **robots.**



{Jason Epstein wants a machine that could print any book ever written.}

Jason Epstein worked in book publishing for more than 40 years. He was editorial director of Random House and founded Anchor Books, the *New York Review of Books*, the Library of America, and the Readers Catalog. Now in retirement, he wants to reconstruct publishing digitally, as digitization is re-creating the music industry.

I became a publisher by accident. When I entered Columbia College in 1945, I was only 17, but I found myself surrounded by veterans in their 20s, some still in their flight jackets and peacoats, many of them married, some with infants. Most of them were in a hurry to find careers and get on with their lives. Some, however, were incipient scholars, and I was fascinated by their worldly talk of Marvell and Donne, Pascal and Voltaire, James and Proust, and Joyce and Eliot. Some of my elders became my friends. For four years we formed an intense coterie of which I was the chief beneficiary because I joined it knowing nothing and acquired from it the rudiments of an education. I had no thought of a job, much less a career in business, certainly not one in book publishing. Thus it did not occur to me that my friends, thanks to the GI Bill, belonged to a large, unprecedented, and undiscovered market for serious books—a new phenomenon in the cultural and commercial life of the United States.

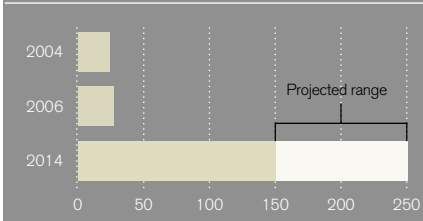
ILLUSTRATION BY MARCO VENTURA

In September 1950, after wasting a year in graduate school, I was on my own financially. For want of a better plan, and with only the vaguest idea of what a book publisher actually did (I had recently seen a film called *The Scoundrel*, starring Noël Coward, about the ruin of a glamorous but dissolute book publisher), I applied to Doubleday's training program, which promised to indoctrinate prospective publishers by rotating them through various departments. Although Doubleday's personnel manager insisted that I was unsuited for the program, Ken McCormick, the firm's editor in chief, hired me nonetheless.

In those days, paperback publishing was an offshoot of magazine distribution. Every month a bundle of cheaply printed popular novels, each selling for 25 cents, was delivered along with that

Digital Bestseller

In North America, only 3 percent of book printing is digital. But digital print volume is expected to increase at least sixfold in the next decade.



SOURCE: CASLON

month's magazines to drugstores and newsstands. Last month's unsold paperbacks were then collected, pulped, and reborn as next month's "pulp fiction." I had been at Doubleday for six months, long enough to grasp the essentials of the business, when I proposed to Ken a plan for another kind of paperback. One February afternoon, as we walked across Central Park, I asked, Why not sell paperbacks in bookstores instead of newsstands? We would publish the kinds of serious works that my friends and I had been reading at Columbia, but which were available only in hard covers and at prohibitive prices. These paperbacks could, I said, be more expensive and of better quality than mass-market pulps: we would break even when we had sold 20,000 copies instead of 100,000. Wouldn't it make more sense to sell 20 copies of *The Sound and the Fury* at a dollar than one hardcover at ten?

What I was proposing was a paperback program that would expand the market for publishers' backlists—that is, books that sell year after year and in the aggregate contain nearly all that we think we know about ourselves and the world. In the 1950s, backlists were the life's blood of publishing: the books had recouped their costs, and their sales provided publishers with a steady stream of profit.

Ken agreed and suggested that I talk to people in production and sales and come up with a business plan. We decided to call the new series Anchor Books, after Doubleday's Aldine colophon, with its frisky dolphin wrapped around a weighty anchor. We began by testing the market with 20,000 copies of 12 titles in sturdy paper bindings, priced between 65 cents and $1.25. The first list included Joseph Conrad, Edmund Wilson, D. H. Lawrence, André Gide, and Stendhal. Within a year or two, nearly every publisher in New York and Boston had a line of "quality paperbacks," which bookstores were selling by the millions. The "paperback revolution," as it would be called, had begun.

The essential factors in the success of this format (new to the United States, although European publishers had been publishing quality paperbacks for years) were an audience of serious readers created by the GI Bill and the 3,000 to 4,000 independent booksellers who constituted the retail market for books. Many of these stores were hardly more than gift shops carrying greeting cards, regional titles, and a few bestsellers, but perhaps a thousand booksellers in cities and major suburbs maintained deep backlist inventories and catered to the eclectic interests of sophisticated readers who found their way to the low-rent neighborhoods where many of the shops were located. Our marketing strategy was simple. We put Anchor Books displays wherever we could, hoping that readers would find them and tell their friends. The books sold themselves.

Hankering for a revolution

It was all too good to last. At first I did not notice that the publishing business, along with much else in American life, was being reshaped by the great postwar demographic shift from city to suburb. As their customer base disappeared, so did hundreds of city bookstores with their thousands of backlist titles. Today, there aren't 50 independent retailers in the United States that stock 100,000 titles or more. By the mid-1960s, the new retail market, based largely on suburban malls where the dominant bookstore chains were paying the same rent as the shoe stores next door, could not afford to stock their costly shelves with slow-moving backlist inventories. Turnover was important to these chain outlets. Heavily promoted books by television celebrities and by well-known writers of formulaic thrillers and romances were what the chains wanted. Very soon, thousands of backlist titles were going out of print every year.

The effect of these new marketing conditions was to turn the industry upside down. Where previously publishers had depended on their backlists, now most of them survived precariously, if they survived at all, by scrambling after bestsellers. Celebrity ephemera were auctioned by their agents for dizzying guarantees, while the powerful retail chains demanded and got ever more discount from publishers, forcing the smaller houses to merge and eventually be subsumed by the conglomerates that dominate the industry today. Publishers continued to produce as many books of real merit as ever, but as Calvin Trillin put it, their shelf life had deteriorated to somewhere between that of milk and yogurt. Book publishing began more and more to resemble the mass-market-magazine business.

In 1958, I left Doubleday for Random House. My arrangement was unusual. For many years I was the firm's editorial director, but I was also free to pursue my own ventures. By the mid-1980s, I had started a few successful businesses for the same readers for whom I had created Anchor Books. I began to look for ways to bypass the marketing forces that were eroding publishers' backlists. In 1986, with this problem in mind, I conceived the Readers Catalog, a directory of some 40,000 backlist titles that could be ordered through an 800 number (the Internet had not yet been commercialized). The idea was to re-create a medium-sized independent bookstore in the form of a printed catalogue the size of a big-city telephone directory. Sales were brisk—but my business plan was flawed. The average revenue per order was about $35, plus shipping and handling, but the cost of handling small orders was more than could be recouped. By the time the Internet was flourishing, I had decided not to put the Readers Catalog online but instead auctioned it off to Amazon.com and Barnes and Noble—warning them that their margins would not cover the cost of handling small orders for individual customers. They have since lost millions of dollars while performing an invaluable service to publishers, writers, and readers.

It was in the aftermath of the failure of the Readers Catalog that I saw the solution to the prohibitive expense of physically handling thousands of low-cost items. Books, like music, are among the few commercial products that can be reduced to digital files, stored, located, and transmitted electronically at virtually no cost. Publishers had been trying to sell elec-

tronic versions of their titles online since the early 1990s, but had failed because the programs were poorly designed and because most readers resisted the idea of reading books on their computer screens or on handheld gadgets. Imprinted paper, folded, gathered, and bound within covers, is still the most durable, readable, portable, and economic medium for books that are meant to be kept. It must be possible, I reasoned, to reconstitute a digital file in the form of a library-quality paperback. What I imagined was the functional equivalent of an ATM—a device that would quickly print a book from a digital file, bind it, trim it, and deliver it to the reader at low cost.

A rudimentary print-on-demand technology already existed, consisting of a separate duplex printer, binder, and trimmer, but the equipment was expensive and cumbersome and required skilled operators. It was designed to function within the existing supply chain of the publishing industry, but for printings too small for a conventional high-speed press. I wanted something else—a free-standing, fully automatic machine that would bypass the entire Gutenberg system. A reader would select a file; the file would be transmitted over a secure network; and within minutes, a nearby machine would print a single copy, in any language, at less cost to the reader than a book produced by more conventional means. By eliminating the physical supply chain, with its storage and shipping costs and retail markup, the new technology would offer readers a vastly greater selection of titles than existing technologies.

The 1950s "paperback revolution" in which I had been so bound up wasn't a revolution at all—merely the introduction of a new format within the existing supply chain. I wanted a true revolution, one that would maximize the world market for books and create unprecedented new efficiencies for publishers and authors.

In 1999, I delivered three lectures at the New York Public Library, where I presented my vision of an electronic future and predicted that, sooner or later, such a machine would exist. (I reworked these remarks in my 2002 book *Book Business: Publishing Past, Present, and Future.*)

At the time, the mall chains had reached the limits of their expansion. Accordingly, by the early 1990s, they were being replaced by the so-called superstores, Barnes and Noble and Borders—much larger, free-standing establishments whose promise to carry large backlist inventories was thwarted in many locations by costs that mandated instead the usual books of the moment, along with music, magazines, trinkets, and coffee bars. An alternative retail channel was more urgently needed than ever.

Getting beyond Gutenberg

What I did not know in 1999 was that the book machine I envisioned already existed. The next year, one of my lectures appeared in the *New York Review of Books*, where it was read by my friend Michael Smolens, an entrepreneur also interested in print-on-demand technology. He told me that such a machine was even at that moment making books in a small workshop in Missouri. Its inventor, Jeff Marsh, would welcome a visit from us. (Disclosure: Smolens, a few others, and I are now in business to deploy Marsh's machine.)

At Marsh's workshop we watched a machine, about two-and-a-half meters long and half as high, receive a digital file, adjust itself to the dimensions of the desired book, and transmit the file to a duplex printer. The printed pages were then gathered and bound within a cover produced by a separate, four-color printer. The entire process took about two minutes. The bound, 256-page book was next conveyed to a trimmer and finished, all without an operator.

It was a transcendent moment.

In the electronic future, every text ever published will be recoverable by searching on Google or sites like it *(see "What's Next for Google?" p. 38)*. Booksellers, publishers, and authors themselves will post digital files of texts on their sites or sites of related interest. At their computers, readers will select books from a nearly infinite library of many languages and transmit them to the nearest book machines, where they will collect the printed books at their convenience.

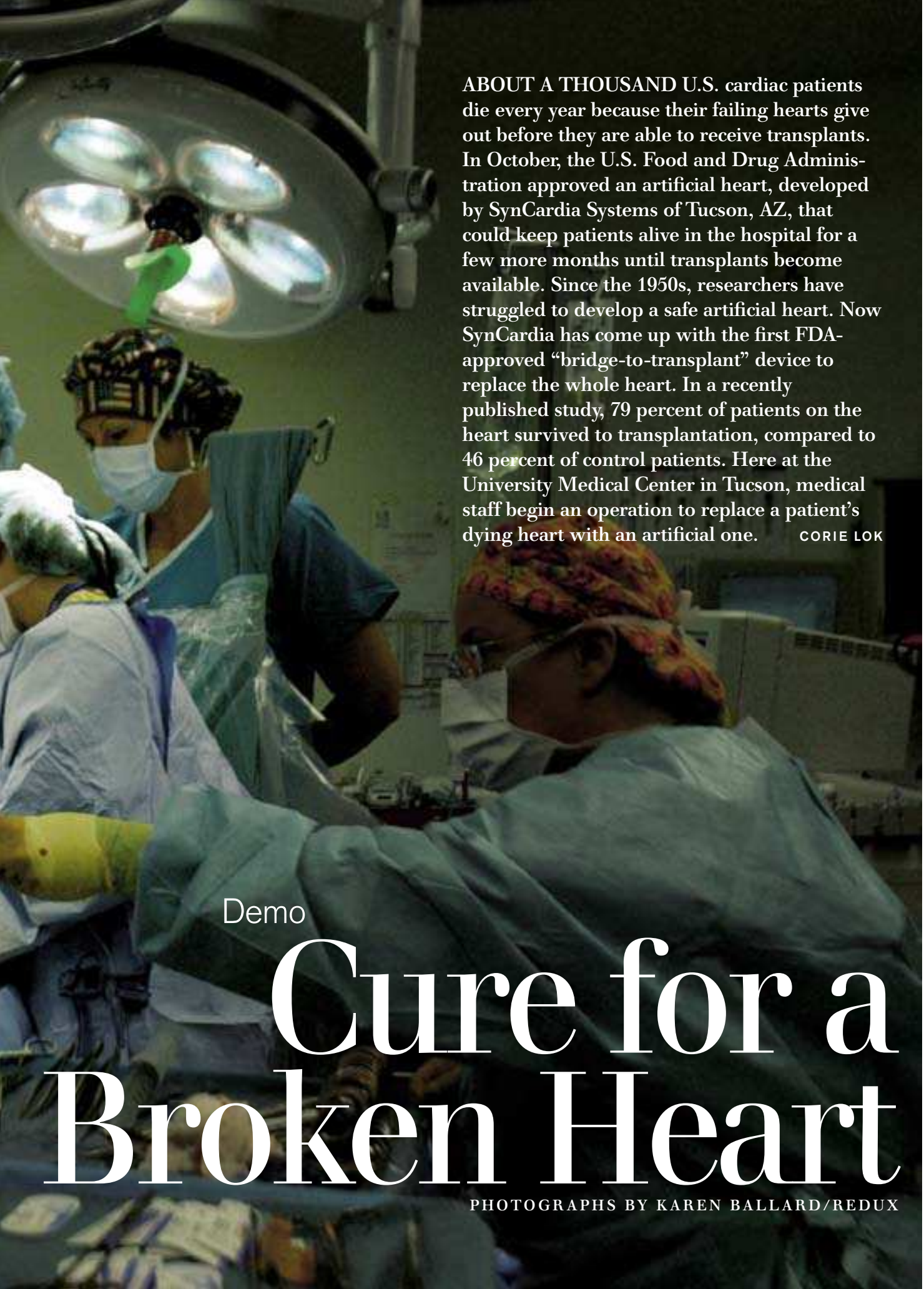
This post-Gutenberg system could be assembled now from existing technologies. But while the technologies exist, the commercial infrastructure to support them does not. Music publishers sell directly over the Internet to consumers who play tunes on devices like the iPod. But before book publishers can sell directly to readers, they will need to deploy thousands of book machines.

One possible solution to this chicken-and-egg dilemma lies in the ability of these new technologies to reach previously inaccessible markets: for example, the 47 million Americans for whom English is a second language and who have no convenient way to buy books in their own language. The beginnings of a viable alternative retail sales infrastructure could be created to service this national market. With this infrastructure in place, publishers could then begin to sell books to English-language readers as well.

Gutenberg thought he could cure the schisms of the 15th century by distributing a uniform missal to all the churches of Europe. Instead, he helped create the Protestant Reformation.

The impact of today's more powerful technologies can scarcely be imagined. What seems to me certain is that these technologies will soon overwhelm the obsolescent Gutenberg system and confront us once again with unprecedented risks and opportunities. ■

{What I imagined was an ATM to print a book.}

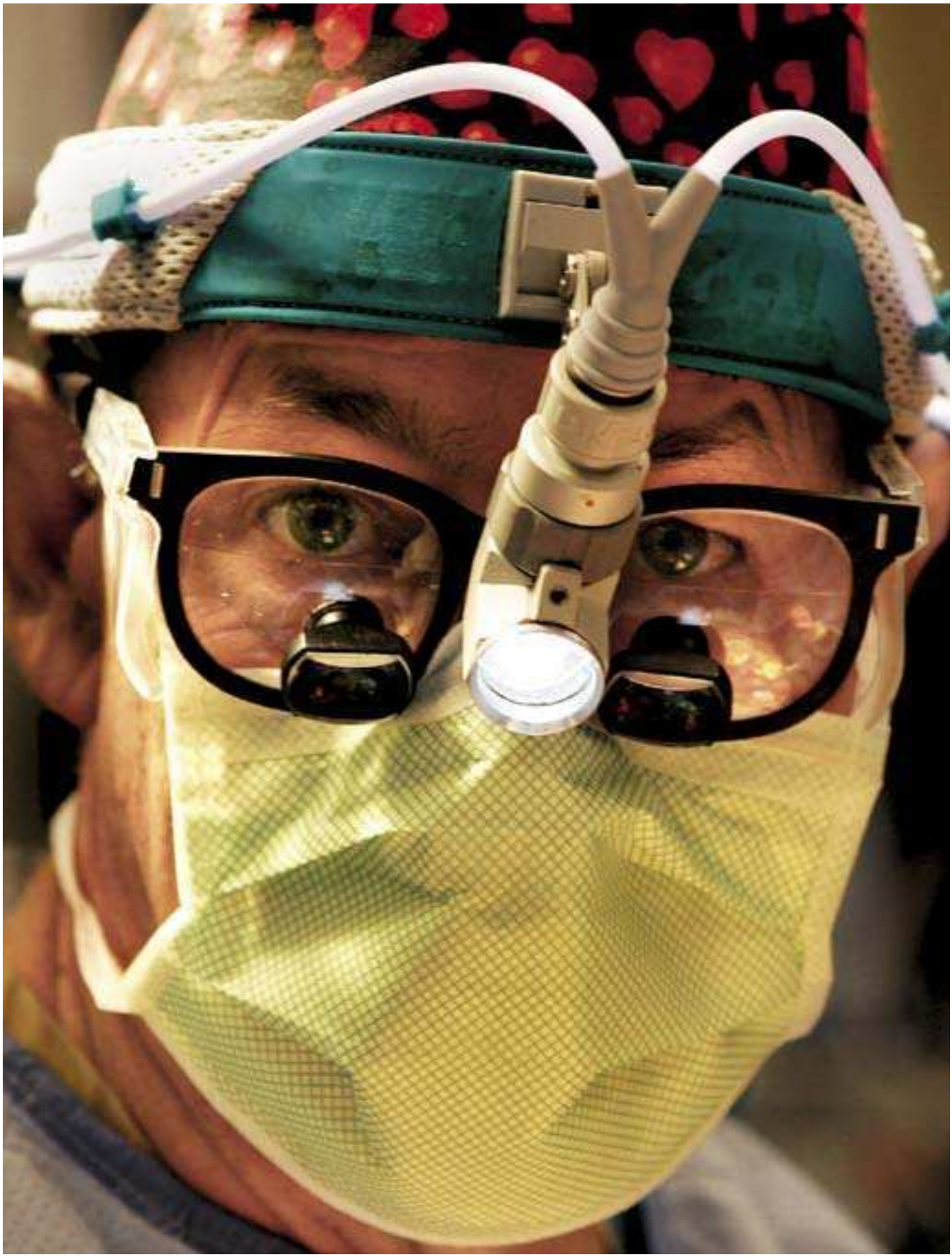


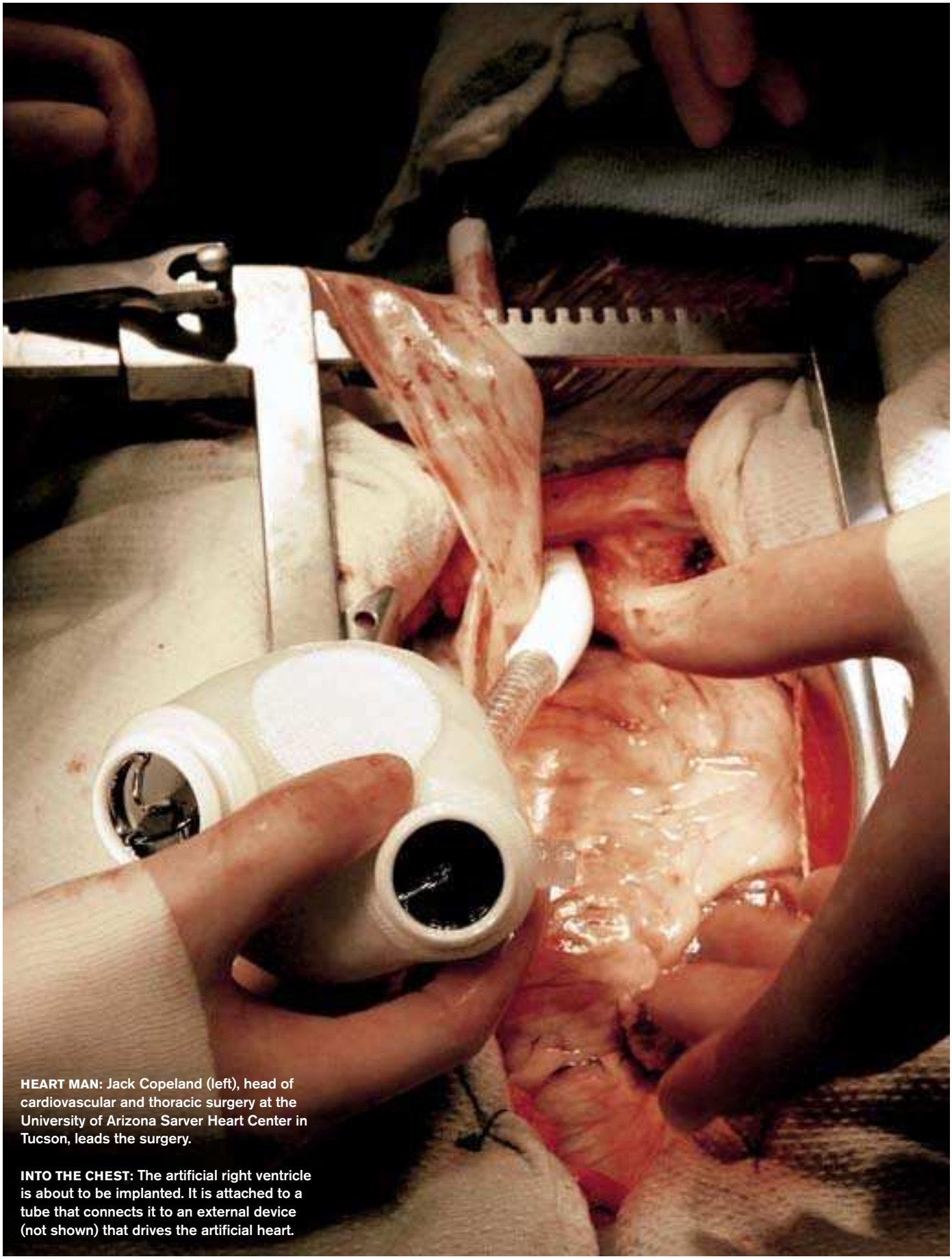
ABOUT A THOUSAND U.S. cardiac patients die every year because their failing hearts give out before they are able to receive transplants. In October, the U.S. Food and Drug Administration approved an artificial heart, developed by SynCardia Systems of Tucson, AZ, that could keep patients alive in the hospital for a few more months until transplants become available. Since the 1950s, researchers have struggled to develop a safe artificial heart. Now SynCardia has come up with the first FDA-approved "bridge-to-transplant" device to replace the whole heart. In a recently published study, 79 percent of patients on the heart survived to transplantation, compared to 46 percent of control patients. Here at the University Medical Center in Tucson, medical staff begin an operation to replace a patient's dying heart with an artificial one. CORIE LOK

Demo

Cure for a Broken Heart

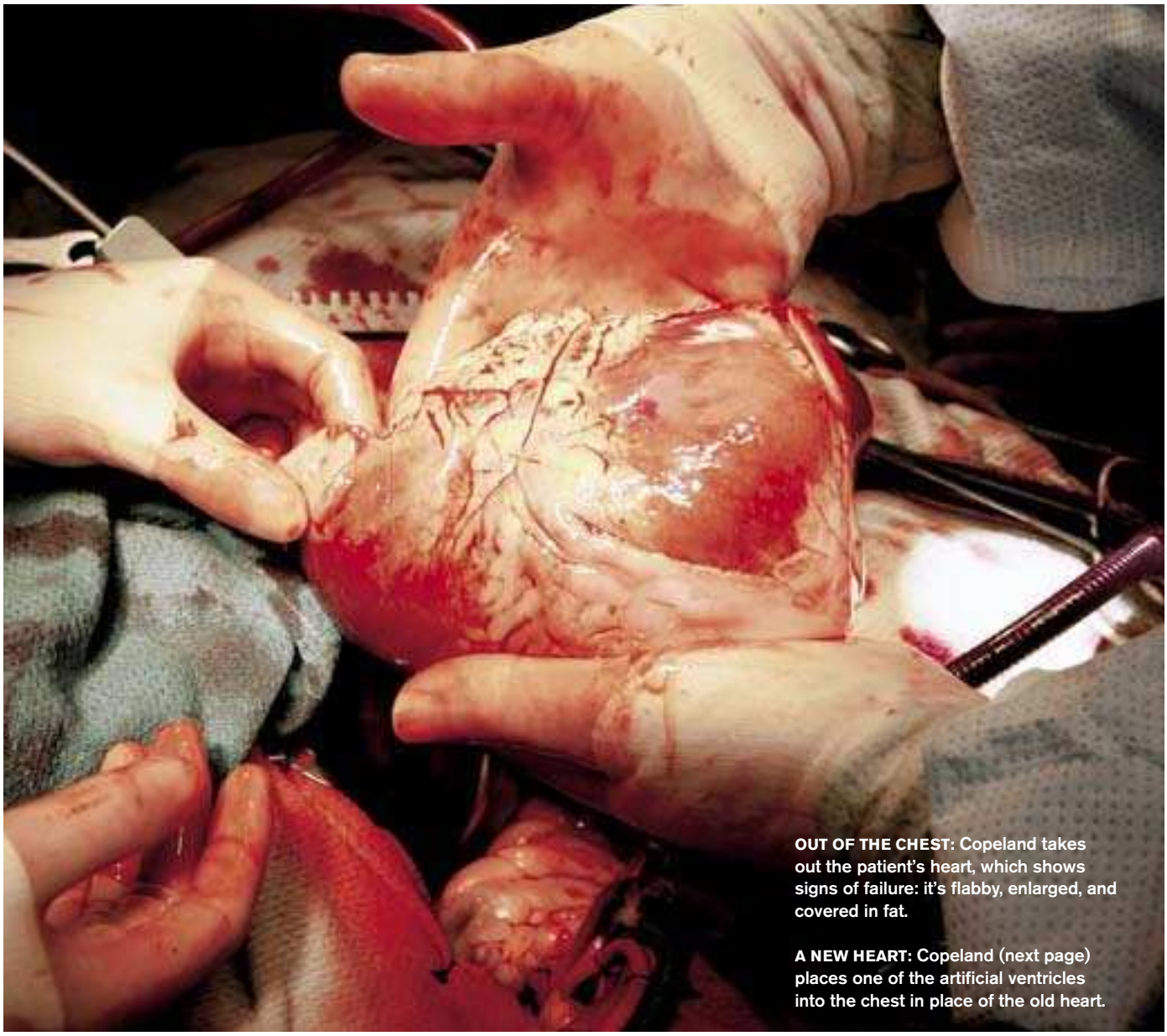
PHOTOGRAPHS BY KAREN BALLARD/REDUX





HEART MAN: Jack Copeland (left), head of cardiovascular and thoracic surgery at the University of Arizona Sarver Heart Center in Tucson, leads the surgery.

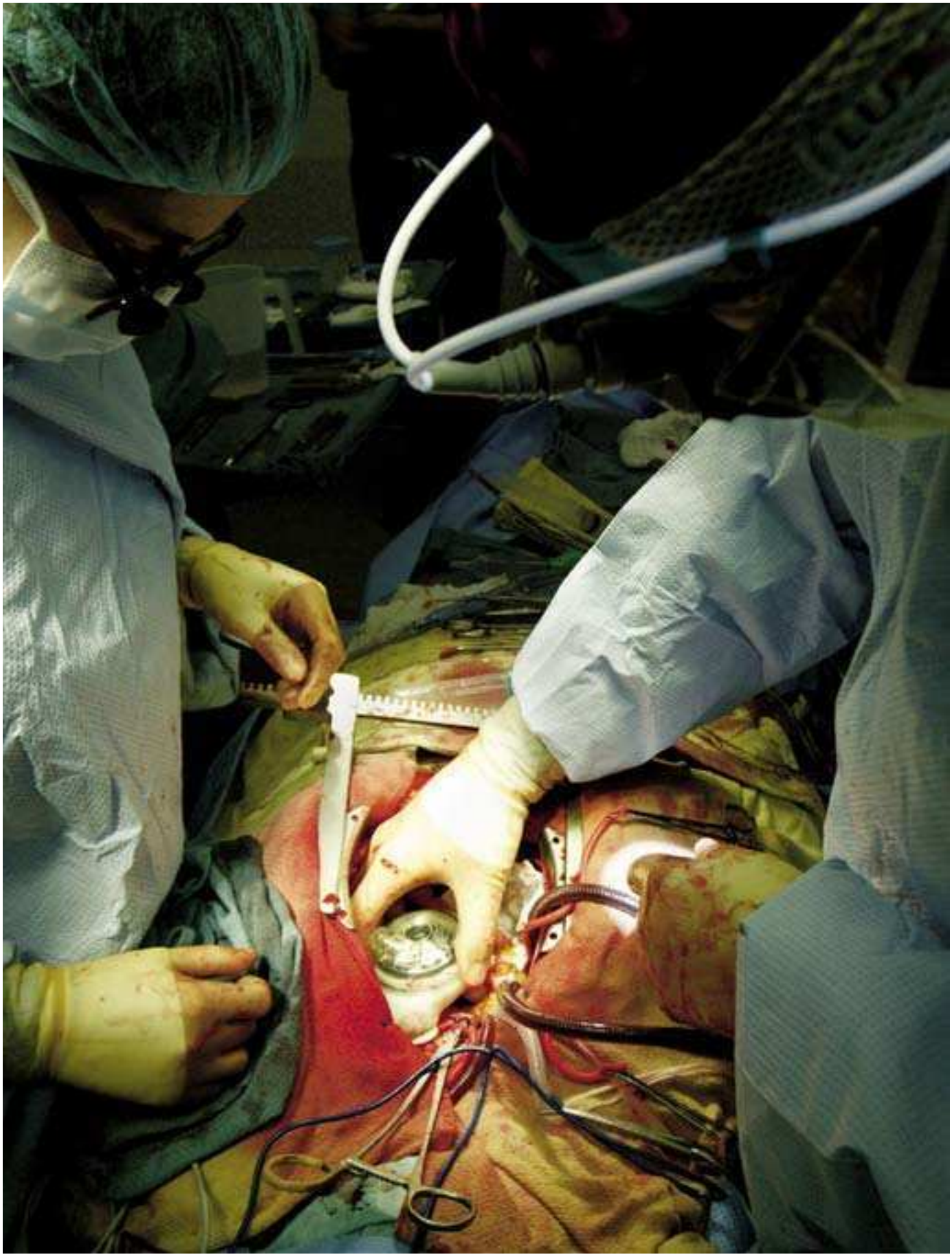
INTO THE CHEST: The artificial right ventricle is about to be implanted. It is attached to a tube that connects it to an external device (not shown) that drives the artificial heart.



OUT OF THE CHEST: Copeland takes out the patient's heart, which shows signs of failure: it's flabby, enlarged, and covered in fat.

A NEW HEART: Copeland (next page) places one of the artificial ventricles into the chest in place of the old heart.

THE PARTS AND THE PATIENT: A prototype (left) of the next-generation device that drives the artificial heart. It's meant to be a portable replacement for the washing machine–sized driver now used in the United States. **SYNCARDIA'S HEART** (middle, left side) is a modified version of the Jarvik-7 heart (right side), which was used in the 1980s but caused problems such as stroke. The FDA placed a moratorium on it in 1990. One of the two ventricles of each heart is shown. **BILL WOHL**, 58 (right), of Scottsdale, AZ, was on SynCardia's heart for about five months before getting a transplant in February 2000. At the 2004 Australian Transplant Games, he won nine medals in cycling, swimming, and track and field.



THERE'S NOT ENOUGH ART IN OUR SCHOOLS.

NO WONDER PEOPLE THINK

LOUIS ARMSTRONG

WAS THE FIRST MAN TO WALK ON THE MOON.

It's a long way from the Apollo Theatre to the Apollo program. And while his playing may have been "as lofty as a moon flight," as *Time* magazine once suggested, that would be as close as Louis Daniel Armstrong would ever get to taking "one small step for man."

Instead of a giant leap, Louis Armstrong delivered one giant free-form crazy jazz groove for mankind.

But as the jazz musician of the 20th century, giant leaps were simply a matter of course for Satchmo. For no one has ever embodied the art form the way he did. It was he who helped make virtuoso solos a part of the vocabulary. It was he who was honored with the title "American goodwill ambassador" by the State Department. It was he who was the last jazz musician to hit #1 on the Billboard pop chart.

Armstrong left his fingerprints on the jazz world, wearing hair-up infords.

Not bad for a kid whose first experience with the trumpet was as a guest in a correctional home for wayward boys. If only today's schools were as enlightened and informed as that reformatory was.

Alas, the arts are dismissed as extravagant in today's schools. This, despite all the studies that show parents believe music and dance and art and drama make their children much better students and better people.

If you feel like your kids aren't getting their fair share, make some noise. To find out how, or for more information about the benefits of arts education, please visit us on the web at AmericansForTheArts.org. Just like the great Louis Armstrong, all you need is a little brass.

There's plenty of brain to go around. Give more to art.

ART. ASK FOR MORE.

Ad Council

For more information about the importance of arts education, contact www.AmericansForTheArts.org.

AMERICANS for the ARTS

Digital Dandies

From function as fashion to fashion as function

Some technologies are tools, others are toys, and still others are attitudes. A case in point is the 7280 cell phone just introduced by Nokia. The 7280 is the size and shape of a candy bar. It's unusual not so much for what it has—a built-in 640-by-480-pixel camera and voice recognition—but for what's missing. The work of Nokia's Mobile Phones Business Group, the 7280 has no keypad at all. Numbers and names are entered by voice only and are displayed on-screen at a fraction of the size of those on conventional instruments. If less is more, the price is nice, too: about $600 retail.

Unhappy with this design philosophy? A separate Nokia division, Vertu, has just the instrument for you—a personal project of Nokia's design vice president Frank Nuovo. The top-of-the-line Signature has a keypad. It also has 18 jeweled bearings, spring-loaded with microscopic rubber bands for what Vertu's website calls "the perfect click." The display is made of what Vertu says is the largest sapphire crystal ever offered on the market. The earpiece is made of aerospace ceramic for a warm touch, while the logo is deposited in a vacuum chamber for permanence. The Signature bezel is offered in platinum and gold; the platinum version sells for an eyebrow-raising $32,000.

But despite all the refinements of the Signature, the 7280 is the more radical technology. Transcending functionality, it is the instrument of the digital dandy. The Vertu is visibly luxurious, but conventionally so. Its buyer is the clockwork connoisseur, the admirer of solidity and complexity. Clockwork connoisseurship first flourished in the 18th century, when the artisans of London and Paris produced not only clocks and scientific instruments of the greatest refinement but also home furnishings with hidden drawers and compartments—more for aristocratic one-upmanship than for security.

In 19th- and 20th-century watchmaking, dandyism diverged from connoisseurship, giving us wafer-thin Patek Philippes on one hand and, on the other hand, self-winding Rolex GMTs carved from solid stainless steel, which told the time in two zones. Connoisseurship is masculine, favoring ruggedization and echoing the battlefield in its love of sandblasted and matte finishes. All-black cameras historically sold at a premium over brushed stainless steel, reflecting the obsession of professional combat and candid photographers alike with avoiding telltale glare.

In the early 21st century, most technological objects may be hybrids, but the connoisseur taste tends to favor the analog, the dandy aesthetic the digital. Most high-end audio equipment, for example, reflects clockwork connoisseurship. Black finishes, dials with flywheels, glowing meters, big switches, massive cables—all glory in overengineering. Connoisseurship revels in the triumph of solidity over domesticity. The dandy, on the other hand, is a flâneur, a jaded, narcissistic observer well-suited to the 7280, whose screen becomes a mirror when not in use. The dandy's car is a near-silent hybrid, the connoisseur's a Hummer.

MICHAEL WITTE

The industrial world of the 19th century and most of the 20th belonged to the connoisseurs. The baby boomers, far from being culturally revolutionary, may have been the last connoisseur generation, closer to their parents than to their children, who have replaced the floor-standing speakers of the 1960s with the earbuds of MP3 players.

And to connoisseurs' chagrin, the market has rewarded dandyism. Consider the Sony Vaio 505 notebook computer, introduced in 1997. Teiyuu Goto, its designer, reportedly insisted on a profile of less than an inch and a magnesium-alloy case at a time when the competition was still using plastic. After some concessions to Sony engineers, Goto held the line at 22 millimeters in thickness, even though an imperceptible additional millimeter could have doubled the hard drive's storage capacity. Despite or even because of this, the 505 was an outstanding success.

At Apple Computer, Steve Jobs spent hundreds of thousands of dollars making the sides of his impractically cubic NeXT machine precisely perpendicular. While the NeXT's hardware could barely support its sophisticated operating system, and the platform subsequently vanished, it ultimately gave Jobs the tools to restore Apple's finances and éclat (the Mac OS X was built from the NextStep OS). Apple's current icon, the iPod, is a dandy technology with the solidity, storage capacity, and ergonomics that make it appealing to all but the most diehard connoisseurs.

The 7280 is within the reach of the affluent young; the Signature is for the prosperous and perhaps socially anxious middle-aged. The 7280 reflects the glories of rapid electronic obsolescence; the Vertu denies death—its own, and its owner's.

I'd love to have it both ways. I'd love to think that a solid key click builds character. But dandies don't mind what they're losing. They can always discard the current model when engineers catch up to designers' visions. "Stand out like a flame in the darkness," urges the Nokia website. Dandies may sometimes burn good money, but they light the way for the rest of us. ■

Our reviews use any artifact—a book, a product, a government report, a movie, a research paper, even an event—as the occasion for a contemplative essay on some technological controversy.

Technology and Happiness

Why more gadgets don't necessarily increase our well-being

JAMES SUROWIECKI

In the 20th century, Americans, Europeans, and East Asians enjoyed material and technological advances that were unimaginable in previous eras. In the United States, for instance, gross domestic product per capita tripled from 1950 to 2000. Life expectancy soared. The benefits of capitalism spread more widely among the population. The boom in productivity after World War II made goods better and cheaper at the same time. Things that were once luxuries, such as jet travel and long-distance phone calls, became necessities. And even though Americans seemed to work extraordinarily hard (at least compared to Europeans), their avid pursuit of entertainment turned media and leisure into multibillion-dollar industries.

By most standards, then, you'd have to say that Americans are better off now than they were in the middle of the last century. Oddly, though, if you ask Americans how happy they are, you find that they're no happier than they were in 1946 (which is when formal surveys of happiness started). In fact, the percentage of people who say they're "very happy" has fallen slightly since the early 1970s—even though the income of people born in 1940 has increased, on average, 116 percent over the course of their working lives. Nor is this a uniquely American phenomenon: you can find similar data for most developed countries. Perhaps the most striking example of progress having little impact on what economists call people's sense of "subjective well-being" is Japan. Between 1960 and the late 1980s, Japan's economy was utterly transformed, as the nation went from a low-cost supplier of cheap manufactured goods to what is perhaps the world's most technologically sophisticated society. Over that stretch, the country's GDP quintupled. And yet by the late 1980s, the Japanese said they were no happier than they had been in 1960.

Even more strikingly, life seems worse for a significant minority of citizens in the rich world. Since the 1950s, reports of major depression have increased tenfold, and while much of that increase undoubtedly represents a new willingness to diagnose mental illness, there's a general consensus among mental-health experts that it also reflects a real development. People are more anxious, trust government and business less, and get divorced more often. In the 1960s Tom Wolfe confounded those who fretted about the gloominess of American life by insisting that Americans were in the midst of a "happiness explosion." Forty years later, plenty of people would disagree.

There is, though, one group of Americans that is imperturbably sunny: the Amish. Their depression rates are negligibly low relative to the rest of society's. Their happiness levels are consistently high. The Pennsylvania Amish, when asked how much they agree with the statement "You are satisfied with your life" (using a scale of 1 to 10), turn out to be as happy as the members of the *Forbes* 400. The Amish, though, do without most of what we think of as modern technology. They don't rely on the automobile, don't need the Internet, and seem to prefer stability and permanence to the heady growth that propels innovation and the U.S. economy. The comparison is a little facile (the Amish have a

You Can't Always Get What You Want

"Does Economic Growth Improve the Human Lot? Some Empirical Evidence," an essay by Richard Easterlin

From **Nations and Households in Economic Growth: Essays in Honor of Moses Abramovitz** Edited by Paul A. David and Melvin W. Reder, Academic Press, 1974

ISTVAN BANYAI


AMISH
NEWS
mini cooper

lot of other characteristics that make people cheerful, including strong community ties, stable families, and religious faith). But it suggests an interesting question: is it possible that technology, instead of liberating us, is holding us back? Is technological progress merely a treadmill, and if so, would we be happier if we stepped off of it?

Can we trust people to know what makes them happy?

The relationship between happiness and technology has been a perennial subject for social critics and philosophers since the advent of the Industrial Revolution. But it's been left largely unexamined by economists and social scientists. The attention that they have paid to the subject of happiness has involved the more capacious relationship between broad material prosperity and well-being. Gregg Easterbrook's book *The Progress Paradox* grappled with this question directly. The economists Bruno Frey and Alois Stutzer published an academic survey of the subject in *Happiness and Economics* in 2001. But the truly groundbreaking work on the relationship between prosperity and well-being was done by the economist Richard Easterlin, who in 1974 wrote a famous paper entitled "Does Economic Growth Improve the Human Lot?" Easterlin showed that when it came to developed countries, there was no real correlation between a nation's income level and its citizens' happiness. Money, Easterlin argued, could not buy happiness—at least not after a certain point. Easterlin showed that though poverty was strongly correlated with misery, once a country was solidly middle-class, getting wealthier didn't seem to make its citizens any happier.

Considering how many decisions about new technology are based on little evidence, it seems plausible that people can get stuck with technologies that don't make them happy but are hard to get rid of.

Easterlin's work did not get much attention when it was first published, but its implications were profound. By suggesting that there was no direct link between wealth and well-being, Easterlin was challenging some basic assumptions of mainstream economics. Most economists begin with the idea that people act in their own self-interest most of the time, and that they usually understand that self-interest pretty well. The choices people make, therefore, must be better than the alternatives (or else people would make other choices). By this argument, wealth is a good thing because it increases people's options and gives them more freedom to pursue whatever it is they want to pursue. For classical economists, it was almost tautological to say that the wealthier people are, the happier they are, too.

Easterlin's relatively simple study suggested that if what people said about themselves was to be believed, you could give people more choices and more wealth and not have much of an impact on their sense of well-being. "Well-being is actually the central idea of economics," says Alan Krueger, an economist at Princeton University. "But we've never really tried to measure it. We've used proxies, and we've said, 'If we're richer, and we have more options, we must be better off.' But we haven't tried to find out if that's really true."

One response to this, of course, is to say that you can't really trust what people say about themselves in surveys, no matter how well executed. Pay attention to what people do, and you'll get a real sense of what they want. On this view, worrying about whether people say they are happy with the choices they make is nonsense. Of course they are. If people spend a lot of money and time buying and using personal computers and wireless phones and personal digital assistants, then these gadgets must make them happy.

There is an inherent logic to this argument, and it has the great virtue of not asking economists to decipher people's motives. But in the last decade or more, deciphering people's motives (or at least their behavior) is something more economists have become interested in doing, and to great effect. Behavioral economists have moved away from assumptions about individuals' perfect rationality in order to develop what they think of as a more realistic model of economic behavior. They've explored the idea, hardly radical outside economics but pretty radical inside it, that people might sometimes make mistakes, and that their decisions (whether individual or collective) could actually make them unhappy. For instance, behavioral economists have shown that people's preferences are what is sometimes called "time-inconsistent." We would like to save in the long term, but in the short term we'd rather spend. Just as strikingly, behavioral economists have shown that human beings aren't very good at anticipating their own desires. Daniel Kahneman of Princeton University, who won the Nobel Prize in economics in 2002, demonstrated that students, when asked to eat a bowl of their favorite ice cream eight days in a row, had a poor sense of whether they would or would not enjoy the experience.

Considering how many decisions about new technologies are based on little or no concrete evidence and involve guessing about the future, it seems plausible that people can get stuck with technologies that don't make them happy but that are hard to get rid of. Plausible, but not certain: as we'll see, when it comes to the vexed relationship between technology and happiness, certainty is not an easy thing to come by.

"The question of technology": net loss or net gain?

In trying to decipher how technology affects well-being, then, it's worth paying attention to a few things. First, there have been few rigorous studies of the specific relationship between technological change and how people feel about their own lives. So the question "Does more (or better) technology make people happy?" is irreducibly speculative. Second, there is something inherently unstable about people's accounts of their own states of mind. Forget people's uncertainty about what will make them happy in the future; can we even trust that people know what makes them happy now?

Most seriously, thinking about technology is hard because people adapt so quickly to the technologies that are available to them. If you had asked someone in 1870 whether she would be happier if she had a personal vehicle that would give her the freedom to travel hundreds of miles a day, in whatever direction she chose, at relatively little cost; the opportunity to fly across the ocean in a few hours; and the ability to speak to people who were

No matter how dramatic a new innovation is, no matter how much easier it makes our lives, it is very easy to take it for granted. Things that were once miraculous soon seem mundane.

thousands of miles away in real time for a few cents a minute, chances are very good that she would have said, yes, it would make her a lot happier. But today, it's the rare person who gets excited about cars, planes, and telephones. We recognize their utility, but they're also sources of frustration and stress. On balance, most people would say they'd rather have cars and telephones than not, but—and this is what makes thinking about happiness so hard—it's not clear they really make us happier.

This seems to be close to a universal phenomenon. In fact, one of happiness scholars' most important insights is that people adapt very quickly to good news. Take lottery winners. One famous study showed that although winners were very, very happy when they won, their euphoria quickly evaporated, and after a while their moods and sense of well-being were indistinguishable from what they had been before the victory. Psychologists even have a word for the phenomenon: "hedonic adaptation."

So, too, with technology: no matter how dramatic a new innovation is, no matter how much easier it makes our lives, it is very easy to take it for granted. You can see this principle at work in the world of technology every day, as things that once seemed miraculous soon become mundane and, worse, frustrating when they don't work perfectly. It's hard, it turns out, to keep in mind what things were like before the new technology came along. That's why broadband users should occasionally use dial-up: it makes them appreciate just what a difference a high-speed connection really does make.

Does our fast absorption of technological progress mean, then, that technology makes no difference? No. It just makes the question of technology's impact, for good and ill, more complicated. Let's start with the downside. There are certain ways in which technology makes life obviously worse. Telemarketing, traffic jams, and identity theft all come to mind. These are all phenomena that make people consciously unhappy. But for the most part, modern critiques of technology have focused not so much on specific, bad technologies as on what Heidegger called "the question of technology"—that is, the impact of technology on our humanity.

Those critiques have staked out two apparently opposed positions, which nonetheless share a common skepticism about people's ability to use technology to their own ends. The first position, which one can see in the work of the French critic Jacques Ellul or, more oddly, in the novels of Philip K. Dick, is that technological "progress" is leading to an ever more rigid, controlled, soulless society, in which it's easier for people to be manipulated and monitored. The second position, which has been well articulated in books like Neil Postman's *Amusing Ourselves to Death* and Robert Putnam's *Bowling Alone*, is that technology is central to the increasing privatization of experience, which in turn is creating a fragmented, chaotic society, in which traditional relationships are harder to sustain, community is increasingly an illusion, and people's relationships to each other, mediated as they often are by machines, grow increasingly tenuous.

There's obviously something to both arguments. Privacy has become increasingly fragile in a world of linked databases. In many workplaces, technologies like keystroke monitoring and full recordings of phone calls make it easier to watch workers. The notion that technology disrupts relationships and fractures community gained mainstream prominence as an attack on television, but in recent years it has also become central to the critique of the Internet. In *Bowling Alone*, Putnam suggests that TV is a chief culprit in the gradual isolation of Americans from each other and the erosion of the social capital that makes societies run smoothly. Similarly, the deleterious effects of the Internet, which supposedly further isolates people from what critics always call "the real world," were pointed to early on in a famous study of 169 Pittsburgh residents, "Internet Paradox: A Social Technology That Reduces Social Involvement and Psychological Well-Being?" According to the study, published in the September 1998 issue of *American Psychologist*, instead of allowing them to connect with a much wider set of potential friends and exposing them to information they might otherwise never have come across, the Internet instead made people more depressed and lonely than they would otherwise have been.

This broad criticism of technology's impact on relationships is an interesting one and is especially relevant to the question of happiness, because one of the few things we can say for certain is that the more friends and close relationships people have, the happier they tend to be. But the evidence that the Internet or even television fundamentally erodes relationships as opposed to changing them is not especially convincing. For instance, when the authors of that 1998 study revisited the question a few years later, using a slightly different methodology, they arrived at the opposite conclusion, finding that the Net had a slightly beneficial impact on people's sociability, connections with others, and sense of well-being.

Obviously, a technology as wide-ranging and ubiquitous as the Net will have myriad, immeasurable effects. But the Internet is essentially a communications technology, one that, like the telephone, allows people to expand their affective and informational networks. The Net is hardly the ideal public sphere, where

all discussions are rational and everyone agrees on a definition of the common good. But it is a public sphere, and one that crucially functions without gatekeepers.

The dominant critiques of technology have, then, something exaggerated about them. But one way in which technology, as a rule, does make people less happy is in its relentless generation of *newness*. One of the key insights of happiness studies is that people have a very hard time being content with what they have, at least when they know that others have more. Today, technological change is so rapid that when you buy something, you do so knowing that in a few months there's going to be a better, faster version of the product, and that you're going to be stuck with the old one. Someone else, in other words, has it better. It's as if disappointment were built into acquisition from the very beginning (unless you're buying a 70-inch plasma screen, in which case you should be fine for at least a couple of years). There's no way to circumvent this drooping of the spirit, which creates dissatisfaction in the heart of the modern consumer.

Technology à la carte: bad food, but bigger portions

Daily stress, a nagging sense of disappointment, fear that the government knows a lot more about you than you would like it to: if these are some of the ways in which technology reduces people's sense of well-being, how (if at all) does it increase their happiness? This is terrain that is ordinarily left to the cyberoptimists and transhumanists, who believe that technology should be celebrated for the way it remakes and improves our bodies and minds. But setting flights of fancy aside, there is some intriguingly suggestive work about how certain new technologies make people not just objectively better off but also happier.

Even though people may not, despite their new wealth, be happier than they were, they are still as hungry as ever for more time. It's like that old Woody Allen joke: the food may not be so great, but we want the portions to be as big as possible.

In the marketplace, for instance, the Internet has made consumers happier not so much by cutting prices as by expanding the enormous array of choices available to them in a manageable way. In the happiness stakes, expanding consumers' options is really a double-edged sword: consumers do have a preference for variety and novelty, and the more choices you have, the better the chance that you'll find the thing you really want. But too much choice can actually paralyze people, leaving them, paradoxically, worse off.

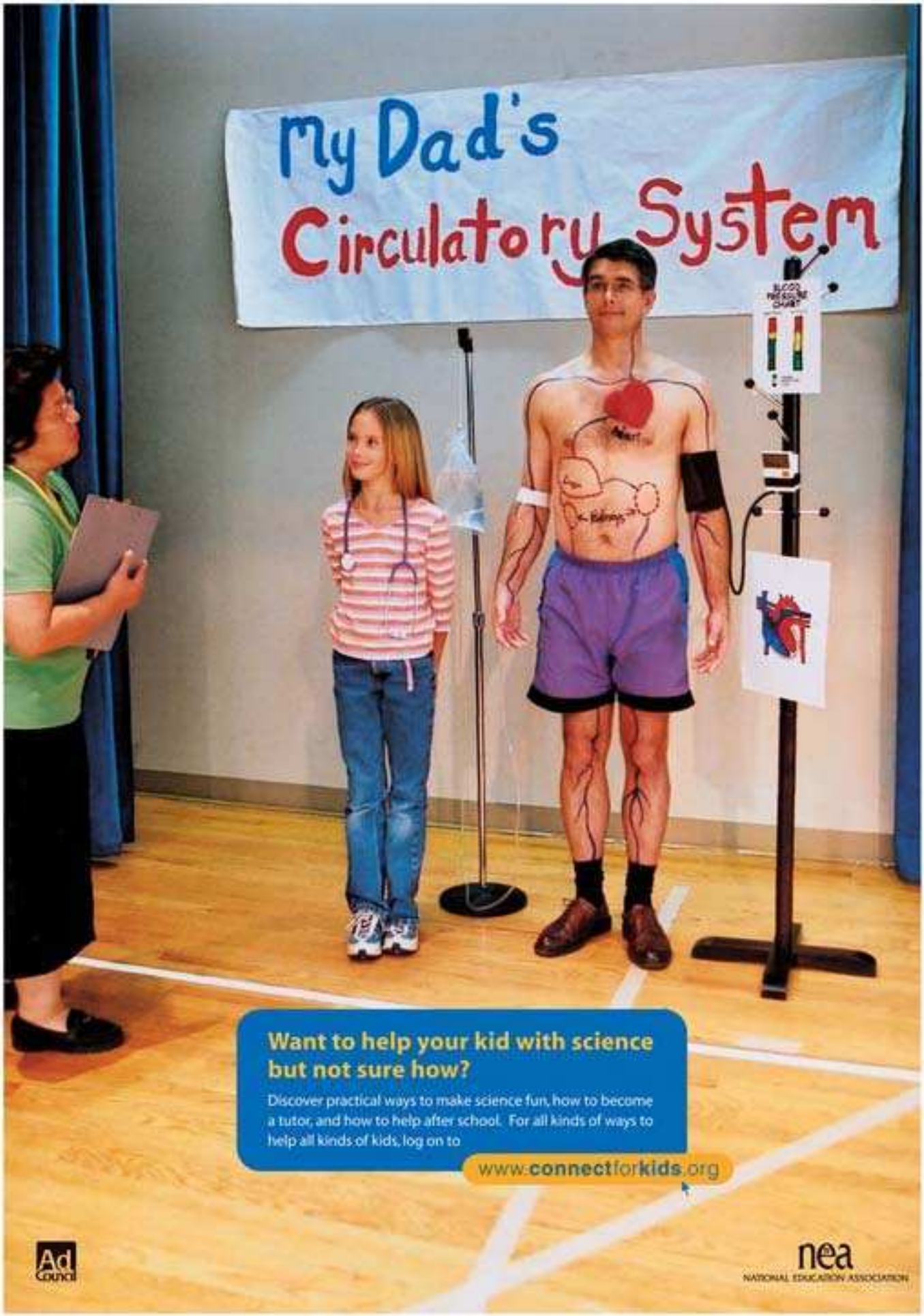
A well-known experiment conducted by Professors Mark Lepper and Sheena Iyengar (at Stanford and Columbia, respectively) illustrates the point: they set up two tables in a supermarket, one with 24 jars of jam and the other with six, and offered discount coupons to anyone who stopped to sample the jams. Of the people who stopped at the 24-jam table, only 3 percent went on to buy jam, while 30 percent of the people who stopped at the six-jam table did. More choices often make people frustrated because they have no reasonable way to navigate through them. What the Internet offers, at least in a nascent form, is a host of mechanisms—collaborative filtering, shopbots, consumer-rating sites—that give people the tools to make informed choices relatively quickly and easily, reducing paralysis and making them happier. The important point here is that among the infinite choices that the Internet offers, one is the option of less choice.

Technology has also radically changed the nature of work, or at least some people's work. This matters because the workplace is central to people's sense of well-being and is more important to them than anything, including family. Studies show that nothing—not even divorce—makes people more unhappy than unemployment. For much of the 19th and 20th centuries, technology's impact on the workplace was ambiguous at best. While the mechanization of agriculture allowed people to escape the farm, it often propelled them straight into heavy industrial labor, which was well paying but often miserable. Technology increased the productivity of workers, but it also diminished their autonomy: superiors controlled more of the details of their working days. Even the office work of the postwar period exemplified by the endless rows of desks in Billy Wilder's *The Apartment* was deeply bureaucratic and controlled. But recently, the rise of the networked society, and the advent of knowledge-based businesses, means that workplaces have become less formal and more open, even while remaining efficient and productive. Already, as Arlie Hochschild points out in *The Time Bind*, a significant percentage of Americans find the atmosphere at work more congenial than the one at home. As the number of knowledge workers grows, and as companies strive to keep them happy, well-being should increase.

The most important impact of technology on people's sense of well-being, though, is in the field of health care. Before the Industrial Revolution, two out of every three Europeans died before the age of 30. Today, life expectancy for women in Western Europe is almost 80 years, and it continues to increase. The point is obvious, but important to note: the vast majority of people are happy to be alive, and the more time they get on earth, the better off they feel they'll be. (Remember, the point about prosperity and happiness is not that prosperity makes people unhappy; it's that it doesn't necessarily make them happier.) Now, the picture is a little more complicated than this. Living a few extra years as a geriatric may not be ideal. But until very recently, life for the vast majority of people was (in Hobbes's formulation) nasty, brutish, and short. Technology has changed that, at least for people in the rich world. As much as we should worry about the rising cost of health care and the problem of the uninsured, it's also worth remembering how valuable for our spirits as well as our bodies are the benefits that medical technology and pharmaceuticals have brought us.

On a deeper level, what the technological improvement of our health and our longevity underscores is a paradox of any discussion of happiness on a national or a global level: even though people may not be happier, even though they are wealthier and possess more technology, they're still as hungry as ever for more time. It's like that old Woody Allen joke: the food may not be so great, but we want the portions to be as big as possible.

Technology may only improve the taste of the meals slightly, but it makes them a lot bigger, and for most of us, that has the promise of something like happiness. ■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Toward a New Vision of Manned Spaceflight

President Bush wants to give NASA a second life. Good.

MARK WILLIAMS

From May 1961, when Alan Shepard became the first American in space, Gene Kranz was the man to have running Mission Control. He was flight director for *Apollo 11*'s Mare Tranquillitatis touchdown in 1969 and *Apollo 13*'s aborted mission in 1970 (and he was played by the actor Ed Harris in the 1995 movie *Apollo 13*).

When I interviewed him in 2001, Kranz decried America's abandonment of manned space exploration. "NASA is not living up to its responsibilities to make space more accessible," Kranz insisted. "If you compare the situation to the development of the U.S., where they moved from the East Coast to the Mississippi and then onwards, it's almost like we've halted at the Mississippi, and we just keep sending the explorers and scouts across, not the merchants, shop owners, and farmers."

For anyone who had participated in NASA's heroic age, it must have been galling that as the 21st century began, the only operational manned spacecraft in which the U.S. had a hand were the shuttle—an expensive Earth-orbiting truck—and a space station a few hundred kilometers above the planet's surface. After all, to reach the moon in 1969, the U.S. space program had crammed an enormous amount of technological innovation into a single decade. In building the Saturn V rockets—3,200 tons and 36 stories tall—and devising Apollo's computer, imaging, and control systems, NASA had invented technologies with wide applications beyond spaceflight. Some of those technologies (like the telecommunications satellite) are vital elements of today's global civilization. If we had sustained this rate of progress, true believers argue, we might have reached Mars by now.

If we're not exploring Mars, they conclude, it must be NASA's fault. Thus, when *SpaceShipOne*, privately developed by aviation pioneer Burt Rutan and Microsoft billionaire Paul Allen, won the $10 million Ansari X Prize after its second ascent to the edge of space on October 4, 2004, some called it a defining moment—a sign that the era of privatized spaceflight had arrived.

If only for Gene Kranz's sake, it would be pretty to think that the flight of *SpaceShipOne* bears comparison to the opening of the American frontier. But a cheap, reliable means of lifting payloads into low earth orbit, 350 to 1,400 kilometers from the planet, remains the *sine qua non* for opening space. To achieve its three minutes at an altitude of 100 kilometers, *SpaceShipOne* traveled at three times the speed of sound. To reach low earth orbit, it would need to travel 10 times faster than that and consume about 50 times as much energy; during reëntry, that energy would have to be dissipated.

No space plane constructed with existing materials could satisfy those demands and still carry enough fuel to power out of Earth's gravity. *SpaceShipOne*, with a novel hybrid engine that used nitrous oxide (or liquefied laughing gas) and hydroxy-terminated polybutadiene (rubber), is a stunt designed to suck in moneyed space tourists and kindle a private manned-spaceflight industry. In those limited terms, it's a success. Following an announcement by Virgin Atlantic Airways chairman Sir Richard Branson about a new space venture called Virgin Galactic, the X Prize Foundation—the St. Louis nonprofit that sponsored the Ansari X Prize—proposed an annual multimillion-dollar event that, commencing in 2005, could become a jaunty mix of Grand Prix car racing and a kind of Olympics for rocket engineers. Meanwhile, Nevada millionaire Robert Bigelow started talking about a $50 million contest, called America's Space Prize, to build spacecraft that could reach orbit and service inflatable orbital modules now being developed by Bigelow Aerospace.

Even without this private-sector activity, 2004 saw revived interest in manned spaceflight. In January, the Bush administra-

Flight Readings

Report of the President's Commission on Implementation of U.S. Space Exploration Policy: A Journey to Inspire, Innovate, and Discover
www.nasa.gov/pdf/60736main_M2M_report_small.pdf

Speech by President George W. Bush, January 14, 2004
www.nasa.gov/pdf/54868main_bush_trans.pdf

New Moon Rising: The Making of America's New Space Vision and the Remaking of NASA
By Frank Sietzen Jr. and Keith L. Cowing
Apogee Books, $33.95

BONESTELL SPACE ART

tion announced a new mission for NASA that included sending astronauts to the moon, Mars, and beyond. Bush-haters dismissed the initiative as a cynical ploy. But in coming decades, even if the private sector can reach Earth orbit with reduced launch costs, the cutting edge of spaceflight—deep-space exploration—will necessarily be the province of expensive, government-funded programs.

The Bush initiative has now defined the goals for one such program. Furthermore, this is the first time any U.S. administration has set forth a policy of *continuing* exploration. The agency's new mission statement fulfills the fondest desires of true believers like Gene Kranz. "The greatest need is for NASA to establish some sense of direction," Kranz said in 2001. "I would like to see a set of goals for the next 50 years and a plan for the next 20, with a Mars mission set for around 2025."

(Re)Ignition

The "Report of the President's Commission on Implementation of U.S. Space Exploration Policy" calls for finishing construction on the International Space Station by 2010, and for continuing research there on how weightlessness and radiation affect human physiology. The shuttle will be retired. By 2008, the U.S. will have developed a new manned vehicle: the Crew Exploration Vehicle, or CEV, which will conduct its first mission no later than 2014 and be capable of transporting human personnel to the International Space Station. Using the CEV, American astronauts will return to the moon between 2015 and 2020. A permanent moon base could exploit the moon's lower gravity for the launching of future spacecraft. Though no exact timetable has been set, Mars is next.

If we're returning to space, it's hardly premature. When Kranz—who still has a high-school term paper he wrote in 1950 called "The Design and Possibilities of the Interplanetary Rocket"—gazes up at the moon on starry nights in the small city near Houston where he's retired, the sight must be bittersweet. The last man to walk on the moon, Eugene Cernan of *Apollo 17*, is now 70. All 12 U.S. astronauts who visited the lunar surface will be dead in another generation. A generation after that, most of the global population alive between 1969 and 1972—when NASA's six moonshots came to seem almost as routine as the Concorde's transatlantic flights—will also shuffle off this mortal coil. The Apollo project will then pass into history, like Egypt's pyramids and medieval Europe's great cathedrals. When Sir Arthur C. Clarke was asked what event in the 20th century he would never have predicted, he spoke for many when he said, "That we would have gone to the moon—and then stopped."

The conventional explanation for why NASA faltered after Apollo is that the U.S. went to the moon for national prestige; once that goal had been accomplished, there was no incentive to go any farther. Yet the fact that NASA rejected technologies that might have furthered manned exploration is evidence that America undertook the space race for reasons other than bragging rights. The U.S. space program was a product of the Cold War, of a planet so militarized that even at its poles, the great radar networks of NORAD and its Soviet counterpart ranged against each other and nuclear subs cruised below the ice. In this context, the U.S.S.R.'s 1957 launch of the satellite *Sputnik* potentially extended the battlefield into space. NASA was formed for purposes of American national survival—not prestige.

By 1962, both sides had rocketed men into orbit. The next beachhead was the moon. Here the U.S. had an advantage. After World War II, Wernher von Braun had brought Hitler's rocketeers to America. German ideas profoundly influenced American conceptions of manned spaceflight.

In a series of articles in *Collier's* magazine in the early 1950s, von Braun inflamed popular anxiety about Soviet intentions for space by describing space stations as platforms for spying and launching nuclear weapons. The space race guaranteed that von Braun—first as director of the U.S. Army's missile program, and then as head of NASA's Marshall Space Flight Center—would see his giant Saturn boosters built. But because national security drove the U.S. space program, von Braun's master plan, in which Saturn rockets would be cannibalized while in orbit and refitted as assembly stations for fleets of interplanetary ships, was discarded by NASA for the lunar-orbit rendezvous scheme chosen for the Apollo program. By landing a couple of astronauts in a lu-

nar excursion module, Apollo offered the fastest route to the strategic high ground.

Apollo remains human history's most brilliant project. Yet in the long term, it offered nothing that made space more accessible. If NASA had gone with von Braun's initial plan, an array of space stations might have been orbiting Earth by the 1970s. And there were other beckoning paths that NASA, shaped by the shifting exigencies of the Cold War, chose not to follow.

For instance, the nuclear-test-ban treaty of 1963 halted the United States' Project Orion, a top-secret effort to develop massive spaceships—on the order of thousands to millions of tons—propelled by nuclear detonations. In terms of its physics, Orion wasn't necessarily insane. Stanislaw Ulam, the coinventor of the hydrogen bomb, had conceived the idea the day after the first U.S. atomic-bomb test in 1945. Project Orion was led by Ted Taylor, designer of the U.S. nuclear arsenal's largest and smallest bombs, and included Freeman Dyson, an architect of quantum electrodynamics theory.

Apollo remains human history's most brilliant project. Yet in the long term, it offered nothing that made space more accessible.

To understand how Orion might have worked, imagine an enormous external-combustion engine. First, a nuclear bomb would be ejected through a hole in the bottom of Orion's hull and detonated. Matter packed around the bomb would become exploding plasma. A thousand-ton aluminum pusher plate, fixed to the ship's stern on giant shock absorbers, would shield and cushion the ship from the blast. The shock would have propelled Orion through space.

Asked today how he could have proposed using several hundred nuclear detonations to launch the Orion spacecraft into orbit 500 kilometers above the earth, Dyson is sanguine: "The worldwide fallout from Orion would have been only about 1 percent of the fallout from atmospheric bomb tests then." Orion would have been a Faustian bargain, but the payoff was raw power: nuclear fission releases a million times as much energy as burning chemical rocket fuel. Dyson, for one, expected to be junketing around the solar system with a crew of 40 by 1970.

Fuel Deficiency

The central claim of Orion still stands today: chemical rockets are ill-suited to deep-space exploration. "Already in 1958," Dyson has written, "we could see that von Braun's moon ships would cost too much and do too little." For chemical rockets, metallurgical physics is destiny. The melting temperature of the engine's alloys limits the velocity of its ejected gas to between three and five kilometers per second. The only way to make a rocket reach even low earth orbit—which takes a velocity of eight kilometers per second—is to use booster stages. By this method, however, lifting one ton of payload into orbit requires about 16 tons of chemical rocket. To make a round trip to the moon, as Apollo did, meant five stages and almost 1,000 tons of chemical rocket for every ton of crewed module.

During the 1960s, NASA declined to pursue either of two strategies that would have made manned spaceflight feasible in the long term. The first was development of von Braun's orbital platforms, where smaller modules lifted out of Earth's gravity could be assembled into larger space-going vessels. The second was the development of an alternative to chemical rockets.

Does NASA's new mission, as framed by the Bush administration, suggest that these lessons have been learned?

New Moon Rising: The Making of America's New Space Vision and the Remaking of NASA, by Frank Sietzen Jr. and Keith L. Cowing, is a book so rushed it seems unedited. Still, it sheds some light, and true believers have reason to be guardedly optimistic. Two major NASA projects, Constellation and Prometheus, will provide the technologies central to achieving the agency's new goals. Constellation will develop several models of the new Crew Exploration Vehicle: the first to carry astronauts into orbit around the earth, the second to travel to the lunar surface, and later versions to reach other planets. An essential part of von Braun's interplanetary strategy is being revived: CEVs may be assembled in Earth orbit. Meanwhile, Project Prometheus will develop a nuclear-powered electric propulsion system that could carry a spacecraft to destinations like Mars.

At first glance, it seems that the technologies that NASA once rejected are being reconsidered. But Freeman Dyson points out that the most important criterion for a nuclear electric propulsion system like that of Prometheus is the weight-to-power ratio, measured in kilograms per kilowatt. To substantially improve on existing chemical rocket systems, Dyson says, the system needs a ratio no greater than five kilograms per kilowatt. Unfortunately, in the current NASA proposal, the Prometheus system would have a ratio of 300 kilograms per kilowatt. "If Prometheus is funded," says Dyson, "it will set back progress in planetary exploring by 20 years. If we are serious about developing a nuclear system, we need a totally new kind of reactor, operating at much higher temperature than existing types." Developing that reactor, he says, will take a long time.

There are other problems. Most significantly, human beings may not be able to survive the levels of cosmic radiation pervading the solar system beyond Earth's magnetic field for the periods demanded by interplanetary missions. Even on the Russian Mir space station and the International Space Station—both within the protective veil of Earth's magnetosphere—weightlessness and radiation have been substantial hazards for astronauts and cosmonauts spending extended time in space. Exposure to cancer-causing cosmic radiation during a three- to five-year round trip to Mars would be equivalent to receiving 25,000 chest x-rays. The Apollo program's proposed tactic for dealing with solar flares—which was to abort the mission and return to Earth—will not be an option. Consequently, NASA researchers in Mountain View, CA, hope to use carbon nanotubes or other nanoparticles *(see "Mitsubishi: Out Front in Nanotech," p. 34)* to detect, diagnose, and treat the cancers and other health disorders inherent in manned spaceflight.

But for prolonged spaceflight, humans would probably require more radical biological enhancements. Future astronauts might differ significantly from their terrestrial kin. This is a long way from the vision of space travel for the masses that was promoted by Gene Kranz and Freeman Dyson. And as with the development of a new reactor, it might take a long time to create these demi-human space-farers. Concerning the future of human beings in space, a Kafka quote might apply: "There is infinite hope. But not for us." ■

The Zen of Airport Kiosks

For frequent fliers, perfect self-service induces mindlessness and painlessness

MICHAEL SCHRAGE

There was absolutely no way I would make my flight. The Heathrow Express had been late, and British Airways' check-in lines were shockingly long. The queues were filled with shrieking children, steamer trunks, and tourists with zero sense of urgency. I was toast.

Jumping the queue was impossible. Pleading for preferential treatment seemed a nonstarter: too American. I looked for help. There, sitting ignored amid the madding crowd, was a machine.

It was a newly installed British Airways automated ticketing kiosk. No waiting. I scurried over and stuck in my American Express card. Seconds later, my name and flight to Munich popped up on-screen. Four or five more touch-screen taps and I was sprinting to security, clutching my boarding pass and receipt. The door closed behind me the moment I boarded my flight.

The *Star Wars* actress and novelist Carrie Fisher once observed that "instant gratification takes too long." For business travelers trapped in airport queues, Fisher's aphorism is no joke. What makes airport ticketing kiosks such godsends is that they are engineered around the two strongest desires of business travelers arriving at the airport: to be mindless and to feel no pain.

Mindlessness is a mantra for every Executive Platinum flier. You don't want to actually think. You just want to do it and be done with it. Immediately. Continental Airlines' mean time for automated check-in is 66 seconds. You only have carry-on bags? Barely 30 seconds.

As a promoter of mindlessness, the ticketing kiosk's superiority to the ATM is obvious. With an ATM, you think about how much money you need and how much you actually have. In contrast, an ATK (airline ticketing kiosk) presents you with choices you either have already made (your itinerary) or don't need to think about (are you carrying any firearms onto your flight?).

Simply swiping a credit card or frequent-flier card into the appropriate slot creates touch-screen requests requiring little effort to answer. There are, sadly, irksome exceptions. American Airlines, for instance, asks you to enter the name of your destination, something American's computers should surely know. Just display what you have on file, damn it, instead of making me enter LGA or ORD.

Which leads us to a critical distinction between mindlessness and painlessness. The Zen state of ATK interaction occurs when mindlessness and painlessness are one: the flier need neither think nor feel to get his or her ticket. An avoidable choice is an on-screen request for information that the flier knows the airline knows, but which the airline is too lazy or incompetent to bake into its ATK. Avoidable choices—having to tell the machine my frequent-flier number or my destination—require both thought and feeling (irritation). Happily, Southwest's no-frills ATK interactions permit the traveler to enter a perfect state of *satori*.

TIM BOWER

You're at Service

Self-service check-in kiosk for British Airways, type 9988, model E01. IBM, 2004.

Where perfect mindlessness and painlessness are not possible, good ATK design allows a choice between the two. The cleverest example of this is the ATK seat map. A large number of airlines, including Alaska, American, and Continental, show you a color-coded chart and invite you to change your assignment by touching a seat. One doesn't mindlessly choose a different seat, of course, but the ability to procure another seat is made painless.

Even the most unctuous ticketing agents can't do that. Human agents are awful at creating mindlessness and painlessness, and increasingly uncompetitive at offering travelers choices. Superior service, not automated ticketing, is the crux of the ATK's value. On a systems level, the rise of the ATK says far less about ruthless "reductions in force" and more about airlines' desires to mass-produce just-in-time convenience.

And yet, I never would have caught my flight if there had been a queue for British Airways' ATK. I prospered because of others' ignorance. Tomorrow's Heathrow will be less forgiving.

I fret that downtime or demand will create queues in front of ticketing machines as unendurably long as those for human agents. I shudder at the thought of flying families burdened by bouncy tots and bulging bags huddling over the ATK for 10 minutes at a time trying to use the seat map to figure out how they'll all manage to sit together on the flight. I know in my heart that they'll be standing in front of me in line at Logan Airport. After all, some forms of mindlessness cannot be conquered.

Will there be ATKs that discriminate between frequent fliers and the masses? Or ATKs that accept only platinum cards? Or charge an extra $5 per ticket to service the cash rich but convenience starved? Please! ■

Synopses

EDITED BY MONYA BAKER

Each month brings new investigative tools, new ideas for revolutionary technology, and revolutionary applications of existing technology. No one can know today which will matter most tomorrow. But these represent *Technology Review*'s best prediction.

INFORMATION TECHNOLOGY

Publishing for All

Democratizing content publication on the Internet

CONTEXT: Maintaining popular websites like Yahoo requires tremendous investment in bandwidth and powerful Web servers—investment that individual Internet users and small organizations can't afford. If a small site's content becomes extremely popular (as happens when a website like Slashdot links to it), its servers can become so overloaded that they can't handle all the requests they receive. The power to publish popular content to large numbers of people on the Internet is thus restricted to large companies. A group of computer scientists from New York University recently put forward a system called Coral to remedy that situation.

METHODS AND RESULTS: Coral allows one computer's burden to be shouldered by many volunteers. In geek-speak, it is a decentralized and self-organizing peer-to-peer Web content distribution network. Users across the Internet volunteer their computers to collectively replicate and store the contents of popular websites. Internet surfers and Web page administrators can access or link to a website through Coral by adding ".nyud.net:8090" to its URL. A novel indexing technique allows Coral to quickly locate and retrieve the requested content. By distributing content so widely, Coral avoids high loads on both the original Web server and on the volunteer computers. A user is thus able to immediately access popular Web pages through the Coral network, even if the original Web server is reeling under heavy traffic.

WHY IT MATTERS: Coral offers the common Internet user large-scale publishing power. The new system distributes the server load across many nodes on the Internet and can easily handle any sudden spikes in demand for a particular website. That means users could host popular Web pages on their home computers over bandwidth-limited DSL or cable Internet connections without exceeding bandwidth or processing capabilities. Although Coral currently serves only static content and requires at least one Coral user to cache, or store, a website's contents before its load spikes, the system offers the little guy a better chance of speaking to a big audience.

Source: Freedman, M., Freudenthal, E., and Mazières, D. (2004) Democratizing content publication with Coral. *Proceedings of 1st USENIX/ACM Symposium on Networked Systems Design and Implementation.*

Keeping a Secret

A laser for quantum encryption

CONTEXT: Even the best communication security can't prevent an unauthorized party from intercepting and attempting to decode a message. Quantum encryption harnesses a feature of quantum mechanics to solve this problem, making it impossible to observe (or tap into) a system without fundamentally disturbing it, and thus being discovered. Designs for quantum encryption systems have proven simple and elegant but so far impossible to build. Now a team led by Hong-Gyu Park at the Korea Advanced Institute of Science and Technology has moved one step closer to finding this Holy Grail, creating a microlaser capable of transmitting quantized light waves that may one day carry messages with greater security.

METHODS AND RESULTS: The laser was fabricated out of the semiconducting material indium gallium arsenide phosphide, chosen because it can be fashioned to emit photons when a current passes through it. The critical lasing component is a "photonic crystal," a perforated disc of the semiconductor that traps photons, ensuring that they are emitted at a single, constant wavelength. The crystal rests on a narrow post large enough to ensure good electrical activity but small enough not to disrupt the crystal's structure. For the first time, the Korean researchers have demonstrated that an electrically activated microlaser can meet these competing needs.

WHY IT MATTERS: For quantum cryptography to work, the creator of a message must be able to encode information in single photons and send them at set time intervals. Intercepting a photon destroys the information, revealing the presence of an eaves-

dropper. However, if a given bit of information requires more than one photon, the message can be intercepted without being detected. Consequently, the laser in a quantum encryption system must reliably convert an electrical pulse into a single photon at a prescribed wavelength. This work falls short of that goal, as it converts each electrical input into multiple photons. But it is an important step toward building new photon sources for optical communication.

Source: Park, H. G. et al. (2004) Electrically driven single-cell photonic crystal laser. *Science* 305:1444-7.

BIOTECHNOLOGY

Same Genes, Different Doses

Distant DNA controls gene activity

CONTEXT: Even in cases where two people share the same gene, they can produce widely differing amounts of the protein the gene codes for. This can lead to differences in physical characteristics, and it can also mean the difference between sickness and health. Segments of DNA called regulatory elements are one factor controlling how much of a particular protein the body produces. While researchers today can use algorithms to pick out genes from sequences of DNA, they have previously been unable to accurately distinguish regulatory elements from other noncoding DNA, let alone match those elements with the genes that they regulate. Researchers at the University of Pennsylvania, led by Vivian Cheung, have found a way to do just that.

METHODS AND RESULTS: Using white blood cells from 94 people, the researchers identified more than 3,500 genes whose expression was similar among relatives but varied widely among people who were unrelated. These patterns of expression were then correlated with patterns of known genetic markers across the genome. Hundreds of genes' expression was linked to particular genetic markers—far more than the number predicted by chance. About four-fifths of these markers were located more than 5,000 base pairs from the genes that they regulated; many were even on other chromosomes. Researchers found that some "hot spot" regions apparently influence the expression of more than 30 genes. In addition, many genes seem to be regulated by more than one region.

WHY IT MATTERS: Researchers can finally study the genetic differences governing gene expression. The hot spots, which Cheung's team calls "master regulators," will help to tease out some of the mysteries that surround gene expression. More immediately, the techniques may allow researchers to use variation within genes and within regulatory elements to understand and treat disease. For years, geneticists have scoured the human genome for genes that contribute to complex traits, like susceptibility to depression or heart disease. Finding factors that control the genes is just as important but much more difficult. Now scientists should be better equipped to find the genetic variations that make a difference in matters of life and death.

Source: Morley, M. et al. (2004) Genetic analysis of genome-wide variation in human gene expression. *Nature* 430:743-7.

On Again, Off Again

A gene comes with a handy switch

CONTEXT: Good health requires more than the right genes; those genes must also be able to switch on and off at the right time. In research involving animals or cell cultures, figuring out a gene's function is much easier when scientists can turn it on at will. Led by Richard Mulligan, a group of researchers at Harvard Medical School and Children's Hospital in Boston have crafted genes that come with an easily controlled on/off switch—a powerful research tool that has the potential to offer a new kind of gene therapy.

METHODS AND RESULTS: The switch consists of a ribozyme, an enzyme made up of RNA. Laising Yen, a postdoc in Mulligan's lab, and colleagues inserted a ribozyme sequence into a gene that coded for an easily detectable protein. Cells with the altered gene made long stretches of messenger RNA; part of the RNA made the ribozyme, while the rest carried instructions for making the protein. The researchers tinkered with different ribozymes, eventually creating ones that were able to chop up the RNA before the protein it coded for could be made. In the cell cultures and living mice containing the ribozyme sequence, protein production dropped to nearly undetectable levels. What's more, the researchers were able to deactivate the ribozyme using certain drugs—essentially turning on the inserted gene by turning off the off switch. Such treatments succeeded in restoring gene expression by up to 50 percent.

WHY IT MATTERS: The researchers imagine creating genetic therapies in which the onset of a physiological condition would activate the genes necessary to manage it. Genetically engineered cells might be able to secrete insulin in accordance with glucose levels, freeing diabetics from constant blood monitoring and insulin injection. For the moment, however, such dreams are far from reality. Closer at hand and still very exciting are discovery techniques that would allow researchers to monitor the effects produced by several genes in a single animal, or to analyze how a gene adjusts to an organism's aging or to different stages of a disease.

Source: Yen, L. et al. (2004) Exogenous control of mammalian gene expression through modulation of RNA self-cleavage. *Nature* 431:471-6.

Drug Bug

Genetically engineered bacteria treat intestinal disease

CONTEXT: Finding ways to get drugs to the right part of the body is a constant challenge for drugmakers. The intestines would seem easier to treat than other areas, as drugs taken orally should eventually arrive there. But a number of promising drugs for the treatment of colitis, an intensely uncomfortable inflammation of the large intestine, become waylaid in the mucus of the small intestine and never reach their target. Now, a group of researchers led by Lothar Steidler from Ghent University in Belgium has genetically modified bacteria to secrete such a drug as they travel through the gut.

METHODS AND RESULTS: The researchers engineered *Lactococcus lactis* so that it would produce trefoil factors, shamrock-shaped proteins that hasten healing and protect the gut from injury. The modified bacteria proved more effective than the purified protein alone at preventing and treating colitis in mice. Outside the body, the bacteria do not survive.

WHY IT MATTERS: The use of genetically modified (GM) organisms as drug delivery devices is moving toward the mainstream. Another GM bacterium produced by these researchers, one that secretes the anti-inflammatory drug interleukin-10, is being tested in European clinical trials as a treatment for inflammatory bowel disease. Other GM bacteria, to be delivered to the nose and vaginal tract, are being studied to prevent infectious disease. Still another may deliver a cancer vaccine. In the 1980s and '90s, recombinant DNA technology ushered in an era of new protein drugs; despite substantial regulatory and technical obstacles, bacteria may prove an effective way to deliver them.

Source: Vandenbroucke, K. et al. (2004) Active delivery of trefoil factors by genetically modified *Lactococcus lactis* prevents and heals acute colitis in mice. *Gastroenterology* 127:502-513.

New Strike against Stroke

Neuronal damage has a new culprit

CONTEXT: Strokes kill neurons by depriving them of oxygen. Without oxygen, neurons have difficulty producing the molecule ATP, their source of energy. This prevents them from performing housekeeping chores, including the important task of pulling glutamate, a message-transmitting chemical, back into the neuron after its message has been received; glutamate keeps sending signals to neighboring neurons, resulting in a deadly influx of calcium ions. However, drugs designed to curb stroke damage by blocking glutamate's effects have shown disappointing results in clinical trials. New research, led by Zhigang Xiong at the Legacy Clinical Research and Technology Center in Portland, OR, shows another strategy that seems more promising.

METHODS AND RESULTS: To make ATP without oxygen, cells use an inefficient method that produces lactic acid and protons as by-products. Neurons using this method become more acidic; they also become more susceptible to damage, but it wasn't clear why. Xiong and his colleagues speculated that acid-sensing ion channels (ASICs) might move calcium into the cell, thereby accelerating neuronal damage. After showing that strokelike conditions activated ASICs, and that ASICs allowed calcium into the neuron, they studied mice lacking the gene for ASIC1a, which is highly expressed in the brain. When subjected to simulated strokes, mice without the gene fared better than mice with it, even when treated with memantine, a drug that blocks the actions of glutamate. The researchers also discovered that small molecules that block ASICs can protect against stroke injury. In rats treated with one such molecule before simulated strokes, the rate of neuronal death was less than half that among untreated rats.

WHY IT MATTERS: Drugs that block ASICs will likely face many of the same challenges as those that block glutamate: they must be administered quickly after a stroke and could have unintended effects on brain function. Nonetheless, small molecules have already shown the capacity to prevent the type of brain damage caused by this newly described mechanism. Thus, these results offer hope against a devastating cause of disability and the third-leading cause of death in the United States.

Source: Xiong, Z. G. et al. (2004) Neuroprotection in ischemia: blocking calcium-permeable acid-sensing ion channels. *Cell* 118: 687-698.

NANOTECHNOLOGY

Extralong Molecules

Carbon nanotubes stretch out

CONTEXT: Little more than a nanometer wide, carbon nanotubes have become superstars of the nano world: unusually strong, electrically conductive, and stable at high temperatures. Fibers composed of nanotubes should outperform those made from any existing material. However, the length of the tubes—most are only tenths of a millimeter long—requires that they be lined up for peak performance. Now, researchers at Los Alamos National Laboratory and Duke University have created nanotubes that are centimeters long, and whose length is checked only by the size of the chamber used to create them.

METHODS AND RESULTS: The Los Alamos team synthesized the nanotubes by flowing ethanol vapors at 900 °C over an iron catalyst spotted onto a silicon wafer. Tubes grew from these catalyst spots; the catalyst was pushed along the wafer surface in the direction of the gas flow. The longest tubes grew to four centimeters as straight lines across the length of the silicon wafer, terminating only at the wafer's edge.

WHY IT MATTERS: Bundles of carbon nanotubes, spun as fibers, have been promoted for applications where high strength and low weight are critical, from sporting equipment like golf clubs or tennis rackets to science fiction dreams of "elevators" extending into outer space. Although the shorter tubes have many promising applications in their own right, bundles of them have failed to perform up to their potential because of weak links between the tubes. Lengthening the tubes reduces these problems, bringing researchers closer to exploiting the remarkable strength and conductivity of nanotube bundles. But the Los Alamos and Duke researchers have done more than advance a technology; they have done the unthinkable, building individual molecules as long as a paper clip.

Source: Zheng, L. X. et al. (2004) Ultralong single-wall carbon nanotubes. *Nature Materials* 3:673-6.

Nanocauldrons

A friendlier route to zeolites

CONTEXT: Minerals called zeolites are essential to industrial chemistry because they help convert crude petroleum into useful chemicals, including the materials used in plastics. By dramatically reducing the cost of petrochemicals, zeolites make everything from pills to pocket protectors more affordable. Now researchers at the University of St. Andrews in Scotland have discovered a way to make these nanostructured minerals that is not only cheaper but also faster, safer, and less toxic.

METHODS AND RESULTS: Zeolites are typically made in hot water at dangerously high pressures. The minerals are riddled with nanometer-wide pores; molecules tucked inside these pores react quickly and cleanly. Chemists create the zeolites through a "condensation reaction," during which mineral precursors encapsulate molecules added as templates, forming a porous solid. Instead of making zeolites in water, Emily Cooper, a chemistry postdoc at St. Andrews, and her colleagues used liquid salts at a relatively low temperature. These liquids are made of charged molecules, or ions, so mineral precursors condense around them directly, eliminating the need for templates. Afterward, the salt ions are removed, leaving a structure with nanometer-sized holes. The recipe yielded five new nanoporous materials; two represented classes that had never been seen before.

WHY IT MATTERS: The standard process for making zeolites is expensive and dangerous, and it requires specialized equipment. With the new technique, even a high-school laboratory should be able to make them. The millions of possible salt compositions produced through this process could result in the creation of families of zeolites with entirely new functions, leading to better and cheaper everyday products.

Source: Cooper, E. R. et al. (2004) Ionic liquids and eutectic mixtures as solvent and template in synthesis of zeolite analogues. *Nature* 430:1012-6.

Gotta Look Sharp

Atomic force microscopy makes electrical measurements

CONTEXT: The rate of corrosion in devices like batteries and semiconductors is often dictated by nanometer-sized imperfections. Conducting atomic force microscopes (AFMs) can image these nanoflaws, but accurately measuring their electrical properties requires knowing how much of the microscope's sharp conductive tip comes in contact with the active surface. Using a mathematical model, Ryan O'Hayre, an assistant professor in the Stanford University Department of Mechanical Engineering, and his colleagues have found a way to indirectly measure this contact area, overcoming a limit of conductive tip microscopy and improving quality control.

METHODS AND RESULTS: Researchers used a platinum-coated AFM tip to monitor the reaction between hydrogen and oxygen at the surface of a polymer fuel cell membrane; the fuel cell was chosen to show that nanoscale measurements can correlate with macroscale results. The rate of the reaction depends on how much force the tip applies to the membrane: the force pushes the materials together, causing them to deform slightly, and thus increases the area of interaction between the two. Crucially, the researchers showed that the area of interaction can be estimated by determining the hardness of the membrane, accompanied by a few assumptions and mathematical tricks. The researchers experimented across three orders of magnitude of force between tip and sample, and their results were all consistent with conventional experiments, making them more credible.

WHY IT MATTERS: Conducting AFM can give nanoscale resolution to electrical measurements of semiconductors, fuel cells, batteries, and other devices. But while it was possible to measure relative changes in properties like conductivity, capacitance, and impedance across the surface of a single sample of material, comparing such measurements between materials had been impossible. Conducting AFM, while capable of finding flaws, could not measure their absolute severity, since different materials interacted with the AFM tip in different ways. This refinement may convert conductive AFM from a research instrument into a useful tool in a number of industries.

Source: O'Hayre, R. et al. (2004) Quantitative impedance measurement using atomic force microscopy. *Journal of Applied Physics* 96:3540-9.

The Vitality of Biotech

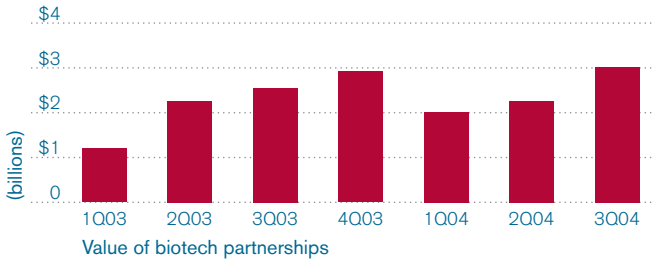
BIOTECHNOLOGY is frequently hailed as the best hope for the discovery of tomorrow's drugs. But how crucial is it to *today's* pharmaceutical industry? Biotech drugs, or biologics, represent more than one-third of the drugs in the earliest phase of research. And in recent years, about one in three novel drugs approved by the U.S. Food and Drug Administration has been a biologic.

Still, among intermediate drug candidates, biologics account for only 8 percent of the new applications for FDA approval and 13 percent of the applications to conduct clinical trials. Yet the number and value of biotech research, development, and licensing deals continue to increase.

As genomics becomes more integrated into drug discovery, and pharmaceutical and biotech companies diversify their drug production, developing both large- and small-molecule drugs, the already murky distinction between the two types of companies will become increasingly irrelevant. **STACY LAWRENCE**

Value of Biotechnology Deals

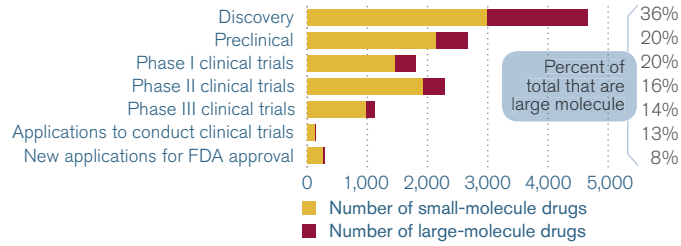
The most recent quarter saw a new high in the value of biotech research, development, and licensing deals.



SOURCE: BURRILL

Number of Biotech and Chemical Candidates

Large-molecule–or biotechnology–drugs account for one in three candidates in the discovery phase of research but only one in seven candidates in phase III clinical trials.



SOURCE: BIOPHARM INSIGHT

Revenue for Pharma and Biotech Companies

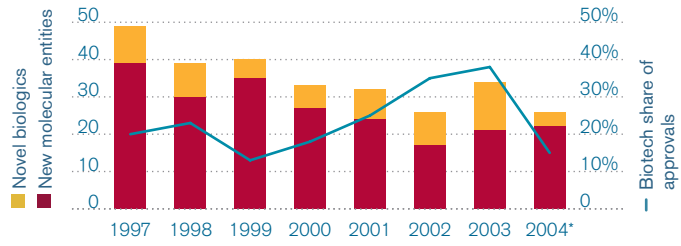
The largest biotech companies are still only a fraction of the size of their pharmaceutical-company counterparts. But increasing diversification within both types of companies makes the distinction increasingly irrelevant.

Pharmaceutical companies	2003 Revenue (millions)	Percent change in 2003 revenue	2003 R&D spending	Percent change in 2003 R&D spending	R&D as a percent of revenue
Pfizer	$45,188	40%	$7,131	38%	16%
Johnson and Johnson	$41,862	15%	$4,684	18%	11%
GlaxoSmithKline	$39,287	1%	$5,114	-4%	13%
Bayer	$34,725	-4%	$2,934	-6%	8%
Roche	$25,611	6%	$3,910	12%	15%
Novartis	$24,864	-14%	$3,756	-5%	15%
Merck and Company	$22,486	5%	$3,178	19%	14%
Bristol-Myers Squibb	$20,894	15%	$2,279	3%	11%
Aventis	$20,719	-4%	$3,470	-9%	17%
Abbott Laboratories	$19,681	11%	$1,734	11%	9%
Top 10 pharma average	$29,532	7%	$3,819	8%	13%
Biotechnology companies					
Amgen	$8,356	51%	$1,655	48%	20%
Genentech	$3,300	28%	$722	16%	22%
Serono	$2,019	31%	$468	31%	23%
Chiron	$1,766	38%	$410	26%	23%
Genzyme	$1,714	29%	$335	9%	20%
MedImmune	$1,054	24%	$156	6%	15%
Gilead Sciences	$868	86%	$165	22%	19%
Biogen Idec	$679	68%	$233	131%	34%
Millennium Pharmaceuticals	$434	23%	$489	-4%	113%
Genencor	$383	9%	$73	3%	19%
Top 10 biotech average	$2,057	39%	$463	28%	29%

SOURCE: REVERE RESEARCH

Novel Chemical and Biological Approvals

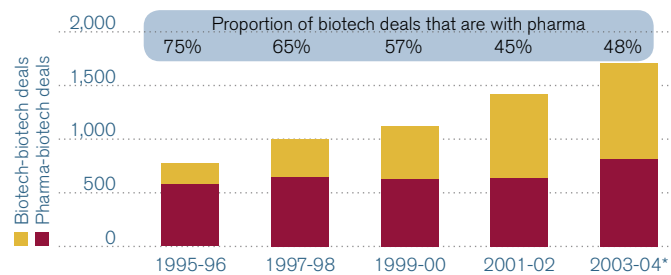
In recent years, biotech drugs have been granted an increasing share of novel-drug approvals. But this year may prove an exception to the trend.



*2004 DATA AS OF SEPT. 30, 2004. SOURCE: U.S. FOOD AND DRUG ADMINISTRATION, CENTER FOR BIOLOGICS EVALUATION AND RESEARCH

Number of Biotechnology Partnership Deals

The pharmaceutical industry has steadily increased its number of research, development, and licensing deals, but its share of the total deals has diminished, as biotechs reach agreements among themselves.



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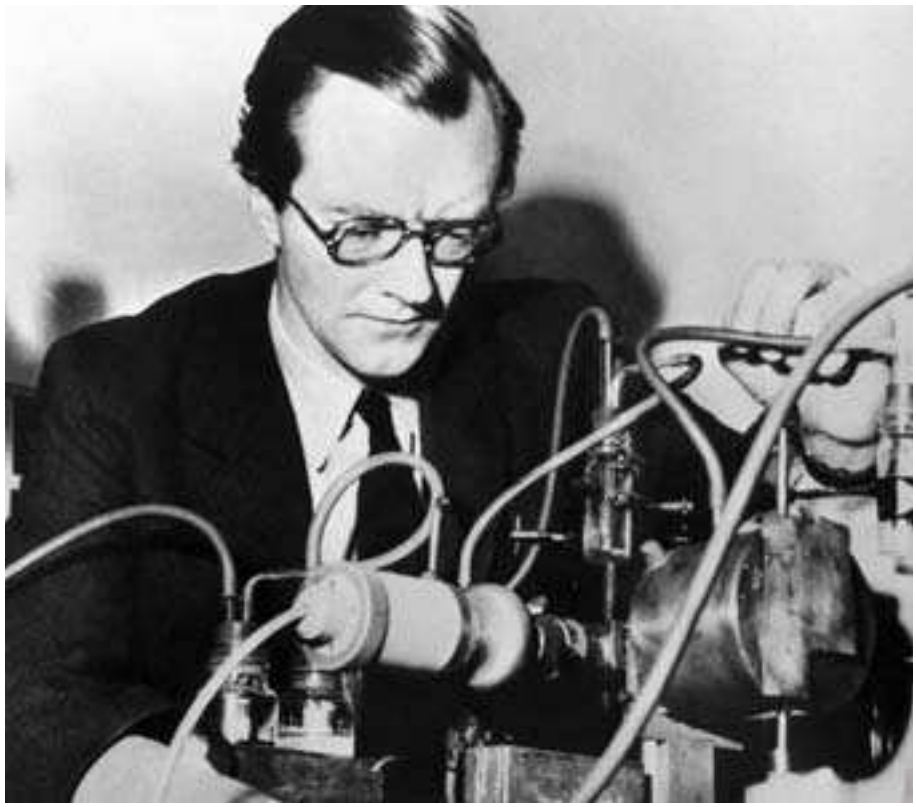

The Third Man

Maurice Wilkins's early fascination with DNA was essential to the discovery of the double helix

ANDREW P. MADDEN

Maurice Wilkins, the biophysicist who died on October 5, 2004, at age 87, was the most reticent and least-known of the three researchers awarded the Nobel Prize in 1962 for the discovery of the double helix, the structural basis of DNA. Wilkins operated in the long shadows of James Watson and Francis Crick, the duo most associated with a discovery that many rank as the most significant, in any field of research, of the 20th century.

If Watson and Crick were the Mick Jagger and Keith Richards of molecular biology, Maurice Wilkins was the field's Charlie Watts, an understated and self-effacing scientist who provided the crucial underpinnings for modern DNA research. Without the early work of Wilkins and his colleague Rosalind Franklin at King's College, London, in the field of x-ray diffraction—an imaging technique that reveals the molecular structure of materials—it is unlikely that Watson and Crick could have made their discoveries. And even after the double helix was revealed in 1953, Wilkins spent the better part of the next decade confirming the finding.

In Watson's bestselling memoir from 1968, *The Double Helix*, he described the moment when Wilkins first showed him an x-ray diffraction image that hinted at the helical structure. "The instant I saw the picture," Watson writes, "my mouth fell open and my pulse began to race."

Controversy would later arise when it was revealed that Rosalind Franklin was responsible for creating the x-ray image, and that Wilkins had shared it without her knowledge. Wilkins never disputed this version of events and admits in his autobiography, *The Third Man of the Double Helix* (2003), that he had been "rather foolish to show it to Jim during our hurried conversation in the corridor." Though Wilkins had a reputation for humility, he was not without competitive instincts. Writing of Watson, he confessed, "Jim later wrote that seeing the pattern had spurred him on tremendously....If I had known that, I might well not have shown him the pattern."

The credit that many felt Rosalind Franklin never received for her contribution to the discovery of DNA would be a source of unease for Wilkins for the rest of his life. But the controversy does little to diminish his own record of achievement.

Like many gifted scientists in wartime Britain, Wilkins, who studied physics at the University of Cambridge, was enlisted to perform military research. He first joined a group of scientists working to develop radar and made contributions that proved valuable to the Allied war effort. In his memoir, Wilkins writes that the radar project gave him his first sense that science could be used to preserve life and hasten the end of the war.

Wilkins's next assignment took him to Berkeley, CA, where he joined the Manhattan Project, researching ways to separate out the particular uranium isotope needed to make an atomic bomb. Though he felt it urgent for the Allies to invent the atom bomb before the Germans, the work also caused him moral unease. But after hearing the concerns of his colleagues, many of whom were refugees who had lost family and friends in Europe, he put his reservations aside.

It was toward the end of his stay in California that Wilkins read *What Is Life?* by Erwin Schrödinger, a quantum physicist and Nobel laureate. As Wilkins put it, Schrödinger linked the "biological idea of a gene with the rather strange world of electrons moving in crystals." Intrigued with the new field of "biophysics," Wilkins set out in his postwar career to apply his training as a physicist to the study of genetics. Wilkins joined King's College, London, in 1946 and remained on the staff there until the day he died.

After the weapons he had helped to create fell on Hiroshima and Nagasaki, Wilkins committed himself to promoting social responsibility in the application of scientific knowledge, later drawing attention to potentially harmful uses of DNA research. He also used his status as a Nobel laureate to advocate for nuclear disarmament and ethical scientific practices. ■

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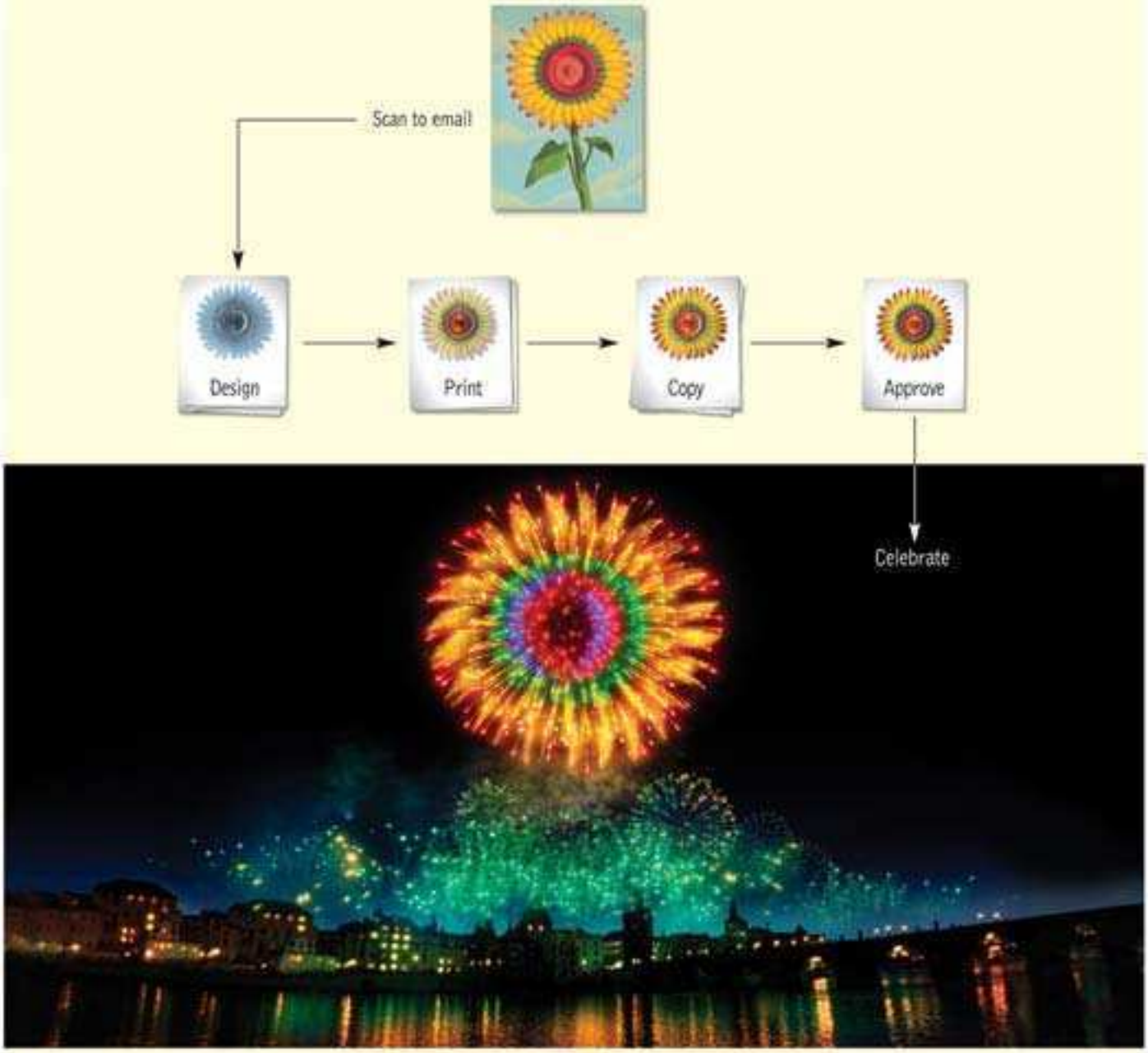

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